DISSERTATION TITLED

"STUDY OF SERUM ZINC STATUS AND GLYCATED HAEMOGLOBIN IN TYPE 2 DIABETES MELLITUS"

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CERTIFICATE

This is to certify that the dissertation entitled **"STUDY OF SERUM ZINC STATUS AND GLYCATED HAEMOGLOBIN IN TYPE 2 DIABETES MELLITUS"** is a bonafide work done by **DR.V.GANESH**, Post Graduate Student, Institute of Internal Medicine, Madras Medical College, Chennai-3, in partial fulfillment of the University Rules and Regulations for the award of MD Branch – I General Medicine, under our guidance and supervision, during the academic year 2013 - 2016.

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DECLARATION

I solemnly declare that the dissertation entitled **"STUDY OF SERUM ZINC STATUS AND GLYCATED HAEMOGLOBIN IN TYPE 2 DIABETES MELLITUS"** is done by me at Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai-3 during 2015 under the guidance and supervision of **Prof. K.S.CHENTHIL, M.D.,** to be submitted to The Tamilnadu Dr. M.G.R Medical University towards the partial fulfillment of requirements for the award of **M.D. DEGREE IN GENERAL MEDICINE BRANCH-I.**

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ABBREVIATIONS

DM	DIABETES MELLITUS
BMI	BODY MASS INDEX
HbA1c	GLYCATED HAEMOGLOBIN
FBS	FASTING BLOOD SUGAR
SBP	SYSTOLIC BLOOD PRESSURE
DBP	DIASTOLIC BLOOD PRESSURE
ADA	AMERICAN DIABETES ASSOCIATION
EASD	EUROPEAN ASSOCIATION STUDY DIABETES
DKA	DIABETIC KETOACIDOSIS
HHS	HYPEROSMOLAR HYPERGLYCEMIC STATE

CONTENTS

INTRODUCTION

INTRODUCTION

Diabetes mellitus is the most prevalent disease worldwide. India will become diabetic capital in the world by 2030. Now it is occupying second place in prevalence after China. Newer concepts and therapy for diabetes is on going worldwide. Trace elements like zinc plays a role in carbohydrate metabolism and affects blood glucose. Study on zinc and other trace elements effect on diabetes is limited.

Both microvascular and macrovascular complications in diabetes are related to oxidative stress. Zinc which has antioxidant property delays diabetic complications. Zinc has a role in insulin secretion from beta cell of pancreas.

Diabetes with zinc deficiency found to have uncontrolled hyperglycemia, insulin resistance and early onset diabetic microvascular and macrovascular complications. Long standing hyperglycemia is measured by HbA1c (glycated haemoglobin).

The study aims to correlate Zinc and HbA1c relationship in newly diagnosed Type 2 Diabetes mellitus. And also to compare zinc relationship with hypertension, obesity (body mass index), dyslipidemia (triglyceride and cholesterol) in diabetes .

AIMS

AND

OBJECTIVES

AIMS AND OBJECTIVES

PRIMARY OBJECTIVES

To study the relationship between serum Zinc level and HbA1C level in newly diagnosed Type 2 Diabetes mellitus.

SECONDARY OBJECTIVES

1. To compare obesity, dyslipidemia, hypertension in diabetes and control.
2. To compare serum Zinc level with obesity , hypertension and dyslipidemia.

REVIEW

OF

LITERATURE

REVIEW OF LITERATURE

History

History of diabetes started around 1550 BC approximately.[19]. A rare disease is mentioned in Egyptian literature , disease that cause patient to urinate frequently and lose weight.

Aretaeus(30-90CE), the great physician named “diabetes” meaning “flowing through”. He noticed a disease with symptoms of increased thirst (polydipsia), increasedurination (polyuria) and weight loss.

Galen (131-201CE) thought patient who complaints of increased urination and thirst are suffering from renal disease . In the 17thcentury Dr. Thomas Willis, a London physician diagnosed patients with diabetes by testing their urine. He would diagnose diabetes if urine taste wassweet . “Mellitus” means “Honey” in Latin. until the 20th century, diabetes were monitored by this method.

Frederic Banting (Canadian medical scientist) and his colleagues discovered an essential harmone called insulin in 1921.The first oral hypoglycemic agent, sulfonylurea was discovered in France by pharmacology professor M.J. Janbon.he noticed lowering of blood sugar in sulfonylurea treated typhoid patients .

Diabetes was first classified into "insulin sensitive" (type I) and "insulin insensitive" (type II) in the year 1950. Later many form of diabetes was recognised.

Aretaeus spoke of diabetes as "the mysterious sickness" 2000 years back. Since then physicians and scientists were contributing their knowledge to diabetes mellitus. And their knowledge made way in discovering wonderful harmone insulin and drug oral hypoglycemic agents. Since then government, doctors and pharmaceutical company working to make patient life easier.

Epidemiology

World

The worldwide prevalence of DM has increased dramatically over the past 20 years. Its prevalence was estimated to 30 million cases in the year 1985 and now it has been increased to 382 million in the year 2013[2]. International diabetes federation projects that diabetes prevalence will reach 592 million by the year 2035. The countries with the greatest number of individuals with diabetes in 2013 are China (98.4 million), India (65.1 million), United States (24.4 million), Brazil (11.9 million) and Russia (10.9 million).

A recent data suggested that diabetes was responsible for almost 8% of deaths or 5.1 million deaths worldwide in 2013. In 2013, it was estimated that 11% of health care expenditures or $548 billion were spent on diabetes patients worldwide.

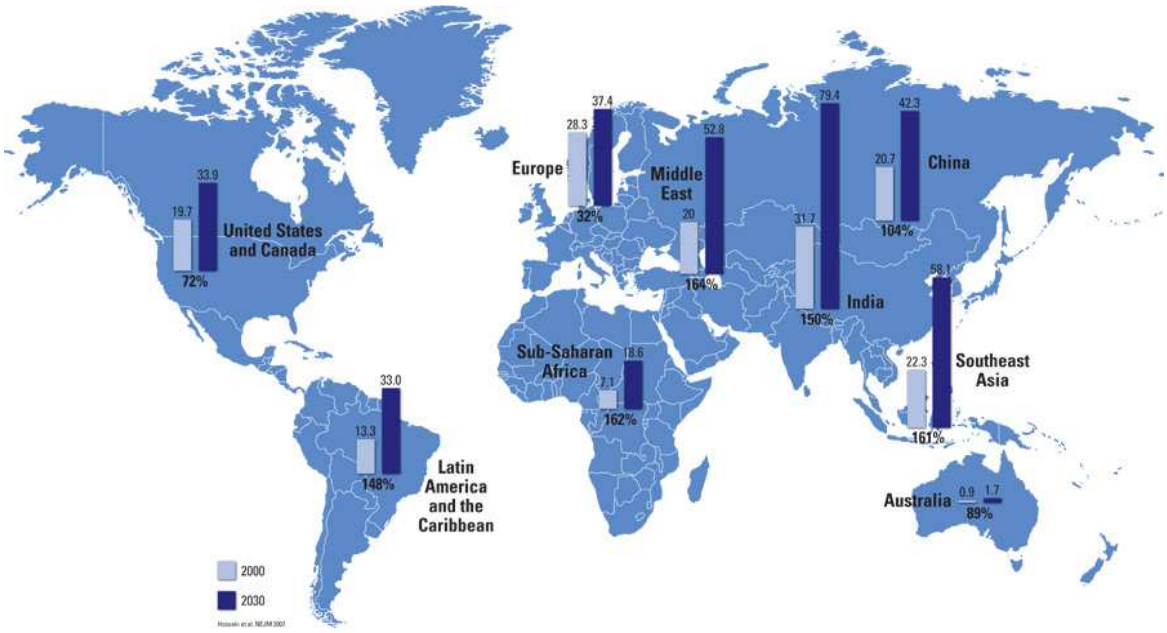


Figure 1 - Worldwide Diabetes Prevalence

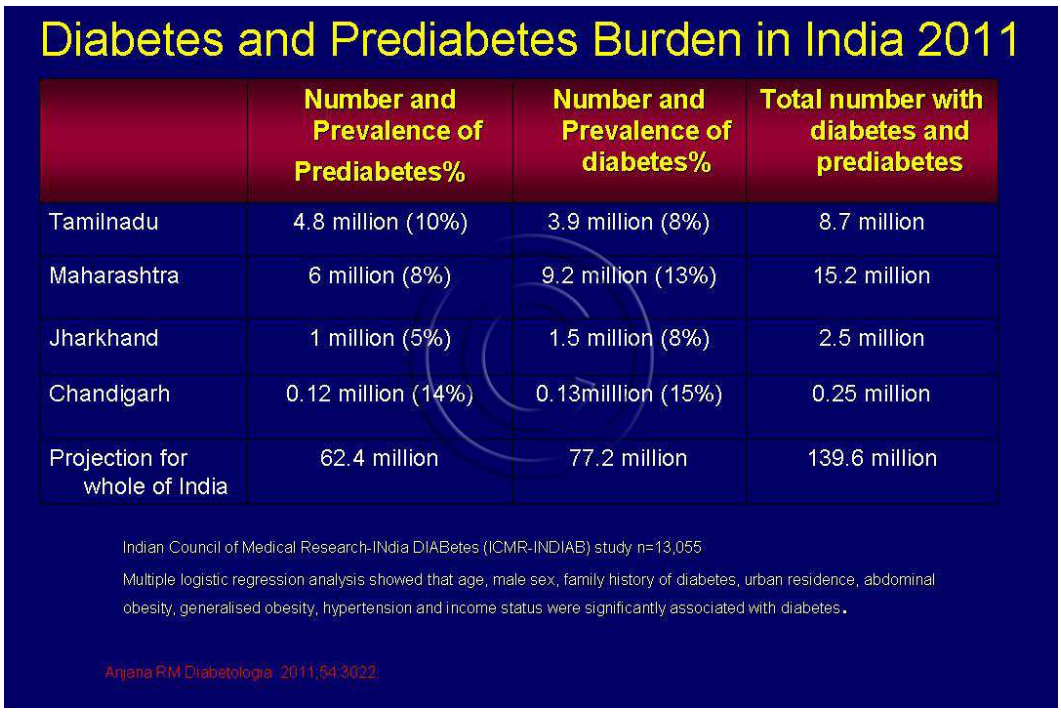
India

In 2013, People lives with diabetes reaches 65.1 million in india. It is estimated diabetes may reach to 101.2 million by the year 2030.[3]

.In 2012 , one million people in india are died due to diabetes. In urban slums of chennai 1 out of 4 people living suffer from diabetes and this is three times higher than national average of about 7%

In india chronic disease is seen in more than 20% of diabetes population and more than 10 % of diabetes population have more than one chronic disease.

Table 1 – Prevalence of Diabetes & Prediabetes



Definition

Diabetes mellitus is a disorder of metabolism characterised by hyperglycemia and it occurs as a result of defects in insulin secretion, insulin action, or both. The chronic hyperglycemiaof diabetes is responsible for long term damage of organs that includes especially eye, kidney, heart, nerves and vessels.

Classification

Diabetes can be classified into the following general categories:

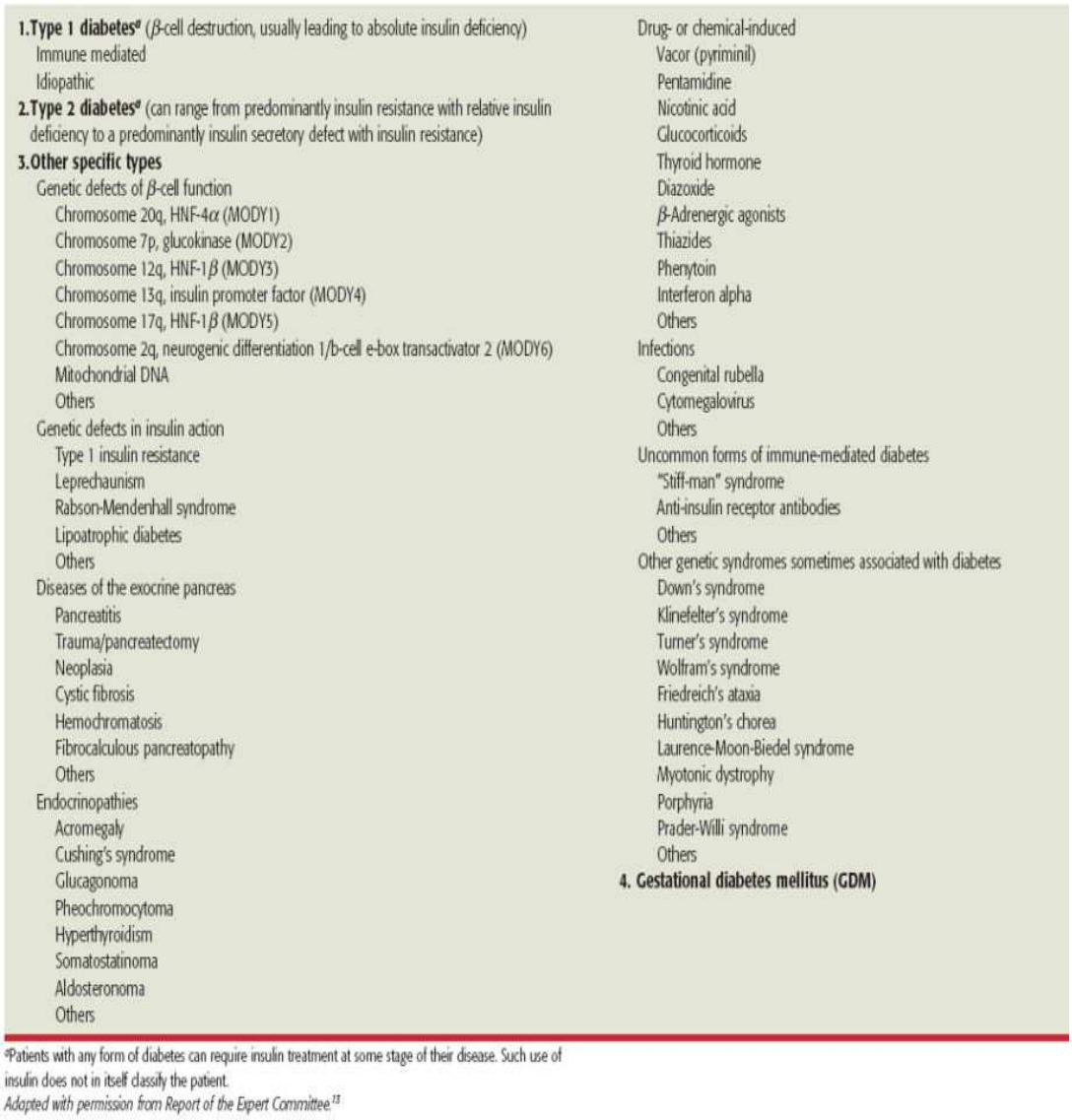
1. Type 1 diabetes mellitus (b-cell destruction, leads to absolute insulin deficiency)

2. Type 2 diabetes mellitus (progressive insulin secretory defect and insulin resistance)

3. Gestational diabetes mellitus (GDM) (diabetes diagnosed in pregnant woman in the second or third trimester that is not clearly overt diabetes)

4. Specific types of diabetes due to other causes:

Monogenic diabetes syndromes (neonatal diabetes and MODY-maturity onset diabetes of young), diseases of the exocrine pancreas (pancreatitis, fibrocalculouspancreatopathycystic fibrosis), and drug induced diabetes (drugs used in treatment of HIV/AIDS or after organ transplantation)



1.Type 1 diabetes[a] (β-cell destruction, usually leading to absolute insulin deficiency)
- Immune mediated
- Idiopathic

2.Type 2 diabetes[a] (can range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance)

3.Other specific types
- Genetic defects of β-cell function
  - Chromosome 20q, HNF-4α (MODY1)
  - Chromosome 7p, glucokinase (MODY2)
  - Chromosome 12q, HNF-1β (MODY3)
  - Chromosome 13q, insulin promoter factor (MODY4)
  - Chromosome 17q, HNF-1β (MODY5)
  - Chromosome 2q, neurogenic differentiation 1/b-cell e-box transactivator 2 (MODY6)
  - Mitochondrial DNA
  - Others
- Genetic defects in insulin action
  - Type 1 insulin resistance
  - Leprechaunism
  - Rabson-Mendenhall syndrome
  - Lipoatrophic diabetes
  - Others
- Diseases of the exocrine pancreas
  - Pancreatitis
  - Trauma/pancreatectomy
  - Neoplasia
  - Cystic fibrosis
  - Hemochromatosis
  - Fibrocalculous pancreatopathy
  - Others
- Endocrinopathies
  - Acromegaly
  - Cushing's syndrome
  - Glucagonoma
  - Pheochromocytoma
  - Hyperthyroidism
  - Somatostatinoma
  - Aldosteronoma
  - Others
- Drug- or chemical-induced
  - Vacor (pyriminil)
  - Pentamidine
  - Nicotinic acid
  - Glucocorticoids
  - Thyroid hormone
  - Diazoxide
  - β-Adrenergic agonists
  - Thiazides
  - Phenytoin
  - Interferon alpha
  - Others
- Infections
  - Congenital rubella
  - Cytomegalovirus
  - Others
- Uncommon forms of immune-mediated diabetes
  - "Stiff-man" syndrome
  - Anti-insulin receptor antibodies
  - Others
- Other genetic syndromes sometimes associated with diabetes
  - Down's syndrome
  - Klinefelter's syndrome
  - Turner's syndrome
  - Wolfram's syndrome
  - Friedreich's ataxia
  - Huntington's chorea
  - Laurence-Moon-Biedel syndrome
  - Myotonic dystrophy
  - Porphyria
  - Prader-Willi syndrome
  - Others

4. Gestational diabetes mellitus (GDM)

[a]Patients with any form of diabetes can require insulin treatment at some stage of their disease. Such use of insulin does not in itself classify the patient.

Adapted with permission from Report of the Expert Committee.[13]

Figure 2 – Classification of Diabetes

Type 2 DM is the most common type of DM . Its prevalence is rising more rapidly due to

Increasing obesity

Dietary intake of processed, energy dense foods

Reduced physical activity

Industrialisation

Aging of population.

Insulin resistance and abnormal insulin secretion are central to the pathogenesis of type 2 DM . Type 2 DM has a strong genetic component than Type 1 DM. The concordance of type 2 diabetes in identical twins ranges between 70% and 90%. Type 2 DM risk increases to 40% if both parents are diabetes.

Clinical features

Most of patients are asymptomatic and hyperglycemia is noted on routine investigation.

Classic symptoms of hyperglycemia seen in DM are polyuria, nocturia, polydipsia, burred vision and infrequently weight loss. Polyuria occurs when glucose in blood exceeds renal threshold that is above 180mg/dl which results in glycosuria. Glycosuria causes osmotic diuresis (polyuria) and hypovolemia (dehydration) which in turn can lead to polydipsia.

Prediabetes

Impaired fasting glucose and impaired glucose tolerance lead to diabetes in future .theseincludes group of people who do not meet the

criteria for diabetes and also doesnot fall in normal. They have high risk of developing diabetes if their glycemic status is not modified by lifestyle.

Significance of Prediabetes

Increased risk of cardiovascular and cerebrovascular diseases.

Predictor of future diabetes mellitus.[4]

.Diabetic range values may be unmasked with stress.

Prediabetes criteria

Impaired fasting glucose 100 – 125 mg/dl. (fasting plasma glucose)

Impaired glucose tolerance 140 – 199mg/dl. (2 hr PG in the 75 g OGTT)

HbA1c 5.7 – 6.4%

Metabolic syndrome

Syndrome X or insulin resistance syndrome

It is characterise by abdominal obesity, dyslipidemia, hypertension and glucose intolerance. Insulin resistance and hyperinsulinemia plays a central role in pathogenesis. It exhibits a proinflammatory state and is

associated with high levels of apolipoprotein B and elevated level of small LDL particles as well as a two foldrisk for developing cardiovascular disease.[5] and a five fold risk for developing type 2 diabetes.

Table 2 – Metabolic Syndrome Criteria

Medscape® www.medscape.com

Risk factors	WHO [3]	NCEP ATP III [5,7]	IDF [8]
	DM/IFG or IGT or IR plus at least two risk factors	Any ≥3 risk factors	Increased WC (ethnicity specific) plus at least two risk factors
Obesity	Waist-to-hip ratio >0.90 in men and >0.85 in women and/or BMI >30 kg/m^2	WC ≥102 cm in men or ≥88 cm in women	WC criteria dependent on ethnicity
Triglycerides	≥150 mg/dl	≥150 mg/dl or drug treatment for elevated levels	≥150 mg/dl or drug treatment for elevated levels
HDL cholesterol	<35 mg/dl in men and <39 mg/dl in women	<40 mg/dl in men and <50 mg/dl in women or drug treatment for reduced levels	<40 mg/dl in men and <50 mg/dl in women or drug treatment for reduced levels
Blood pressure	≥140/90 mmHg	≥130 mmHg systolic or ≥85 mmHg diastolic or drug treatment for hypertension	≥130 mmHg systolic or ≥85 mmHg diastolic or drug treatment for hypertension
Fasting plasma glucose	IGT, IFG, or type 2 DM	≥100 mg/dl or drug treatment for DM	≥100 mg/dl or drug treatment for DM
Microalbuminuria	>30 mg albumin/g creatinine		

Definition of the metabolic syndrome according to different proposals. Adapted with permission [6••]. Criteria for the diagnosis of diabetes mellitus (DM) (each must be confirmed on a subsequent day): symptoms of DM plus casual plasma glucose level greater than 199 mg/dl or fasting plasma glucose level greater than 125 mg/dl or 2 h plasma glucose level after 75 g glucose load greater than 199 mg/dl. NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; IDF, International Diabetes Federation; IFG, impaired fasting glucose (fasting plasma glucose level, 100–125 mg/dl); IGT, impaired glucose tolerance (2 h plasma glucose level after 75 g glucose load, 140–199 mg/dl); IR, insulin resistance; WC, waist circumference.

Source: Curr Opin Rheumatol © 2008 Lippincott Williams & Wilkins

Criteria for diagnosis of Diabetes Mellitus

HbA1c≥ 6.5%. (or)

Fasting Plasma Glucose ≥ 126 mg/dl (7.0 mmol/L). (or)

2 hr Prandial Glucose ≥ 200 mg/dl (11.1 mmol/L) during an OGTT. (or)

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose > 200 mg/dl (11.1 mmol/L).

HbA1c test should be performed using a method that is certified by NGSP and standardised to DCCT assay. Fasting is defined as patient has no intake of calorie for atleast 8 hrs. OGTT test should be performed using a glucose load (75 gm anhydrous glucose dissolved in water) as described by WHO.[6]

In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing .

Screening

Screening of asymptomatic risk individuals plays a important role in reducing morbidity and mortality from diabetes .screening should be done in any person with BMI ≥25 (or ≥ 23 in Asian) with ≥ 1 diabetic risk factor

Risk individuals

1.First degree relative with diabetes

2.Women who delivered a baby more than 9lb or were diagnosed with GDM

3.Hypertensive patient that is BP $\geq$ 140/90 mm Hg or on antihypertensive drugs

4.High risk race / ethnicity

5.Physical inactivity

6.Insulin resistance conditions like obesity, polycystic ovarian syndrome,acanthosisnigricans.

7.HDL cholesterol $\leq$ 35 mg/dl $\pm$ triglyceride $\geq$ 250 mg/dl

8.Cardiovascular disease history

9.Prediabetes

Glycemic targets

HbA1c <7.0 ,preprandial plasma glucose 80 to 130 mg/dl, 2 hr post prandial < 180 mg,dl. Achieving this target helps in reducing microvascular and macrovascular complications. More stringent target is HbA1c < 6.5, less stringet target is HbA1c < 8. Target is based on age /

life expectancy, diabetic durations, hypoglycemic status, individual patient considerations, comorbid conditions and known cardiovascular or microvascular complications.[7]

Treatment of type 2 DM

1. Life style modifications
2. Hypoglycemic Drugs ± insulin therapy.

Life style modifications include eating a balanced diet and regular exercise. Balanced dietconsists of carbohydrate (50-60% of total calories),protein(15 to 20%), total fat(25-35%). Saturated fat should be less than 7% of total calories.Low calorie diet and exercise plays a role in weight reduction as type 2 DM are obese often. Weight reduction decreases insulin resistance and improves glycemic control.

Simple carbohydrates like monosaccharides (fructose, glucose, galactose) and dissacharides (sucrose, maltose, lactose) increase blood gluose rapidly. So diabetic patients should avoid simple carbohydrates. Complex carbohydrates like starch and dietary fibre should be the major form of carbohydrates.[8]

Dietary fibre is not metabolised in small intestine due to lack of enzyme for it. Benefits of dietary fibre include reduce total calorie by

increasing satiety, relieves constipation by increasing bulk of feces, improves glucose tolerance by prolonging gastric emptying and slow absorption of glucose, reduces cholesterol in blood by binding in small intestine and excrete as bile acid.

Gycemic index is the ability of carbohydrate to raise blood glucose. Diabetic patient should choose one low glycemic index food at each meal, combine a high glycemic index food along with low) glycemic food (rice with dal)[9]

Glycemic load is carbohydrate content in food based on glycemic index. Eg potato glycemic index is 80 , 100 gm potato contains 23 gram of carbohydrate so glycemic load is 23x80/100 = 18.

Table 3 –GlycemicIndex and Glycemic Load

Value	Glycemic Index (GI)	Glycemic Load (GL)
High	≥ 70	≥ 20
Medium	56–69	11–19
Low	≤ 55	≤ 10

Food (serving size)	GI	Carbohydrates per Serving (g)	GL	Food	GI	Carbohydrates per Serving (g)	GL
Pastas, Grains, Legumes, Breads, Starchy Vegetables, and Cereals							
Baked potato (150 g)	85	30	26	Corn Chex™ (30 g)	83	30	25
Waffles (35 g)	76	13	10	Corn (80 g)	48	16	8
French fries (150 g)	75	29	22	Popcorn (20 g)	54	11	6
Bagel (70 g)	72	35	25	Cracked wheat (150 g)	48	26	12
Oat bran bread (30 g)	44	18	8	Pancakes (80 g)	67	58	39
White rice (150 g)	56	42	24	Apple muffins (60 g)	44	29	13
Angel food cake (50 g)	67	29	19	Lentils (50 g)	30	40	12
Raisin Bran™ (30 g)	61	19	12				
Fruits, Beverages, and Snack Foods							
Apple (22 g)	38	22	8	Grapes (120 g)	43	17	7
Raisins (60 g)	64	44	28	Apple juice (250 mL)	39	25	10
Banana (120 g)	48	25	12	Tomato juice (250 mL)	38	9	3
Potato chips (28 g)	54	15	8	Plums (120 g)	24	14	3
Jelly beans (28 g)	80	26	21	Chocolate (28 g)	49	18	9
Cherries (120 g)	22	12	3	Sucrose (5 g)	65	5	3

NOTES: Glycemic load (GL) is the glycemic index (GI) divided by 100 and multiplied by its available carbohydrate content (in grams). GL takes the GI into account but is based on how much carbohydrate is in the food or drink tested. GL is numerically lower than the GI of a food or drink.

SOURCE: Foster-Powell K, Holt SH, Brand-Miller JC. International table of glycemic index and glycemic load values: 2002. American Journal of Clinical Nutrition. 2002; 76: 5–56.

Protein has high satiety index, reduce GI of food, slow the gastric emptying time. Daily intake recommended is 1g/kg body weight. Diabetic patients should restrict saturated fatty acids , trans fatty acids and cholesterol. Diets rich in monounsaturated fatty acids decrease insulin resistance.

Diets should include 25 to 35% calorie from fat , recommended is 20% from MUFA(monounsaturated fatty acids), 10% from PUFA(polyunsaturated fatty acids, less than 7 % from SFA (saturated fatty acids). Foods that contains omega 3 fatty acids offer cardioprotective effects.

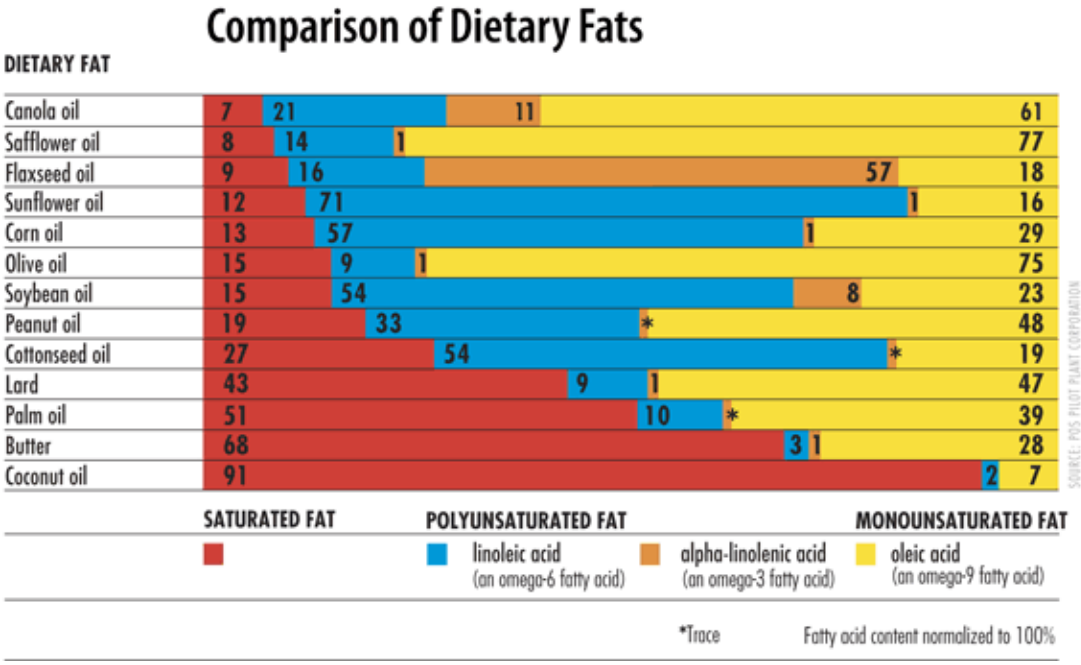


Figure 3 – Dietary fats in various Oil.

Recommended calorie intake in diabetic patient

Obese - 20 Kcal/kg

Normal BMI , sedentary men / women 22 – 25 Kcal/kg

Normal BMI, active men / women - 30 Kcal/kg

Thin / very active - 40 Kcal/kg

Physical activity includes “SAFE” exercise S- strengthening exercise, A- aerobic exercise, F- flexibility exercise, E- endurance exercise.[11]

. Strengthening exercise use muscle strength to move a resistive load (eg, weight lifting and exercise using weight machine).

Aerobic exercise consists of repeated rhythmic continuous movements of large muscle groups (eg walking, cycling, swimming). Recommended timing of aerobic exercise for diabetes is 30 to 40 minutes per day for atleast 5 days a week.

Flexibility exercise aims at improving muscle tone and body control (eg stretch exercise).

Endurance exercise refers to exercise with low intensity and sustain activity for prolonged period(eg cycling, swimming for prolonged period increases cardiorespiratory endurance).

Non weight bearing exercise for people with severe obesity and joint degeneration.

FITT principle should be applied while doing exercise, F (frequency) - 4 to 6 times a week, I (intensity) - to achieve 50 to 80% of target heart rate, T(type) - safe exercise , T (timing) - morning. Brisk

walking is the best aerobic exercise which needs no training and easily done.

Oral antidiabetic agents

Table 4 – Antidiabetic drugs

Class	Mechanism	Agents	Advantages	Disadvantages
Biguinides	Decrease hepatic gluconeogenesis	Metformin	No hypoglycemia, weight neutral	GI disturbance, lactic acidosis
Sulphonylureas	Stimulate insulin secretion	Glimepiride, gliclazide, glibenclamide, etc	Inexpensive	Hypoglycemia, weight gain
Meglitinides	Stimulate insulin secretion	Repaglinide nateglinide	Short onset of action, low postprandial glucose	Hypoglycemia
α-Glucosidase inhibitors	Decrease glucose absorption	Acarbose, voglibose	Reduce postprandial glucose	GI flatulence
Thiazolidinediones	Improve insulin resistance	Pioglitazone	Lower insulin requirements	Edema, CHF, weight gain, fracture, macula edema
DPP 4 inhibitors	Prolong GLP-1 action	Sitagliptine, vildagliptine, saxagliptine, linagliptine	No hypoglycemia	Less clinical experience

Initiate monotherapy depending on patient weight ,glycemic status, and other comorbidities. If not controlled with monotherapy , then try double or triple combination. Finally insulin is added for control of blood glucose.

Insulin

Table 5 – Insulin properties

Insulin Properties				
Insulin	**Onset**	**Peak**	**Effective Duration**	**Maximal Duration**
Rapid-acting insulin				
Lispro (Humalog)	<15 min	1-2 h	2-4 h	3-5 h
Aspart (Novolog)	<15 min	1-3 h	3-5 h	4-6 h
Glulisine (Apidra)	<15 min	0.5-1 h	3 h	3 h
Regular (Novolin R, Humulin L)	0.5-1 h	2-4 h	3-5 h	8 h
Intermediate-acting insulin				
Neutral protamine Hagedorn (Novolin N, Humulin N)	2-4 h	4-10 h	10-16 h	14-18 h
Long-acting insulin				
Insulin glargine (Lantus) analogue	4-6 h	None	24 h	24 h
Detemir (Levemir)	3-4 h	50% in 3-4 h, lasting up to 14 h	5.7-23.2 h	Dose-dependent; 5.7-23.2 h

Complications of diabetes mellitus

Acute life threatening conditions includes hypoglycaemia, diabetic ketoacidosis, hyperosmolarhyperglycemic state. Chronic complications include microvascular and macrovascular disease.

Microvascular complications are diabetic retinopathy, diabetic neuropathy, diabetic nephropathy. Macrovascular complcations are cardiovascular disease (myocardial infarction, ischemic cardiomyopathy

), cerebrovascular disease (ischemic stroke), peripheral arterial disease (gangrene and foot ulcer).

Hypoglycemia

It is defined by ADA and EASD as serum glucose less than 70 mg/dl. An alternate definition is decrease in blood glucose with symptoms of hypoglycaemia. Hypoglycaemia symptoms are neurological changes (altered mental status , seizures, focal deficit) and sympathetic overactivity(sweating, palpitaition , tremor,).

It occurs as a result of medication overdose, diet changes, infections and metabolic changes. Fasting during ramzan, hepatic disease, adrenal insufficiency and starvation are all causes of hypoglycaemia. Drugs like oral hypoglycemic, sulphonamides, insulin, haloperidol, diuretics, salicylates, ethanaol, p-aminobenzoic acid, quinine can cause hypoglycaemia.

Treatment is based on patient ability to take orally. Those who can take orally should be given oral glucose , chocolate followed by complex carbohydrate. Patient who cannot take orally should be treated with intravenous glucose .initially 20 ml of 50 % dextrose bolus and then 5% dextrose at 100 ml/ hr until stabilised. Blood glucose should be monitored frequently until it reaches 100 mg/dl. After stabilising the patient cause of

hypoglycaemia should be evaluated and further management shoud be planned.

Diabetic ketoacidosis &Hyperosmolar Hyperglycemic state

DKA is characterised by triad of hyperglycemia, ketonemia and anion gap metabolic acidosis. It frequently occurs in type 1 DM but can also occurs in type 2 DM in extreme stress such as severe infection , trauma and cardiovascular emergency[11]

.Precipitating factors

Inadequate insulin treatment or noncompliance,

New onset diabetes , insulin pump dysfunction, trauma , surgery,

Acute illness like infection, cerebro and cardiovascular accidents,

Drugs like olanzapine, cocaine, thiazide, terbutaline, steroids, dobutamine

HHS is characterised by hyperglycemia exceeding 1000mg/dl , high plasma osmolality > 380 mOsm/kg , no significant acidosis orserum / urine ketones . It occurs in type 2 DM especially when age is greater than 65 . Restricted fluid intake due to illness , poor thirst response in

elderly, immobility contributes to severe dehydration and hyperosmolality.

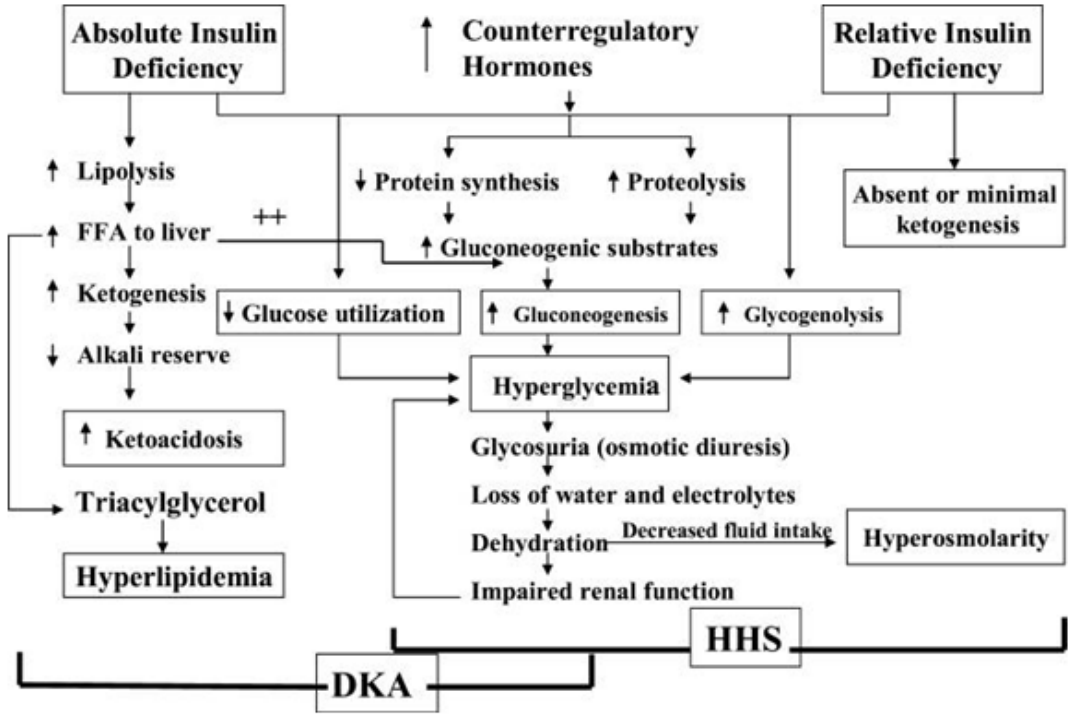


Figure - 4 Pathophysiology of DKA & HHS

Table 6 -Clinical features of DKA & HHS

Diabetic ketoacidosis	Hyperosmolar hyperglycemic state
Develops over 1-2 days	Develops gradually over weeks
Nausea and vomiting	Stupor or coma
Abdominal pain	Profound dehydration
Fatigue and thirsty	Polyuria (several weeks)

Hypotension and tachycardia	Hypotension and tachycardia
Kussmaul respiration, sweet smelly breath	Chronic co-morbidity like dementia, immobility and vomiting
Confusion or drowsiness	Decreased oral intake by concurrent Illness

Table 7 - Diagnostic criteria

Table. Diagnostic Criteria for Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycemic State (HHS)

	DKA			HHS
	Mild	Moderate	Severe	
Plasma glucose (mg/dL)	> 250	> 250	> 250	> 600
Arterial pH	7.25-7.30	7.00-7.24	< 7.00	> 7.30
Serum bicarbonate (mEq/L)	15-18	10-15	< 10	> 18
Urine ketones	Positive	Positive	Positive	Small/absent
Serum ketones	Positive	Positive	Positive	Small/absent
Serum osmolality (mOsm/kg)	Varies	Varies	Varies	> 320
Anion gap	> 10	> 12	> 12	Variable
Mental status	Alert	Alert-drowsy	Stupor-coma	Stupor-coma

Adapted from Kitabchi AE, et al.[3]

Complications of DKA and HHS

Cerebral oedema, pulmonary oedema due to excess fluid, hypoglycaemia, hypokalemia, cortical vein thrombosis.

Treatment of DKA and HHS

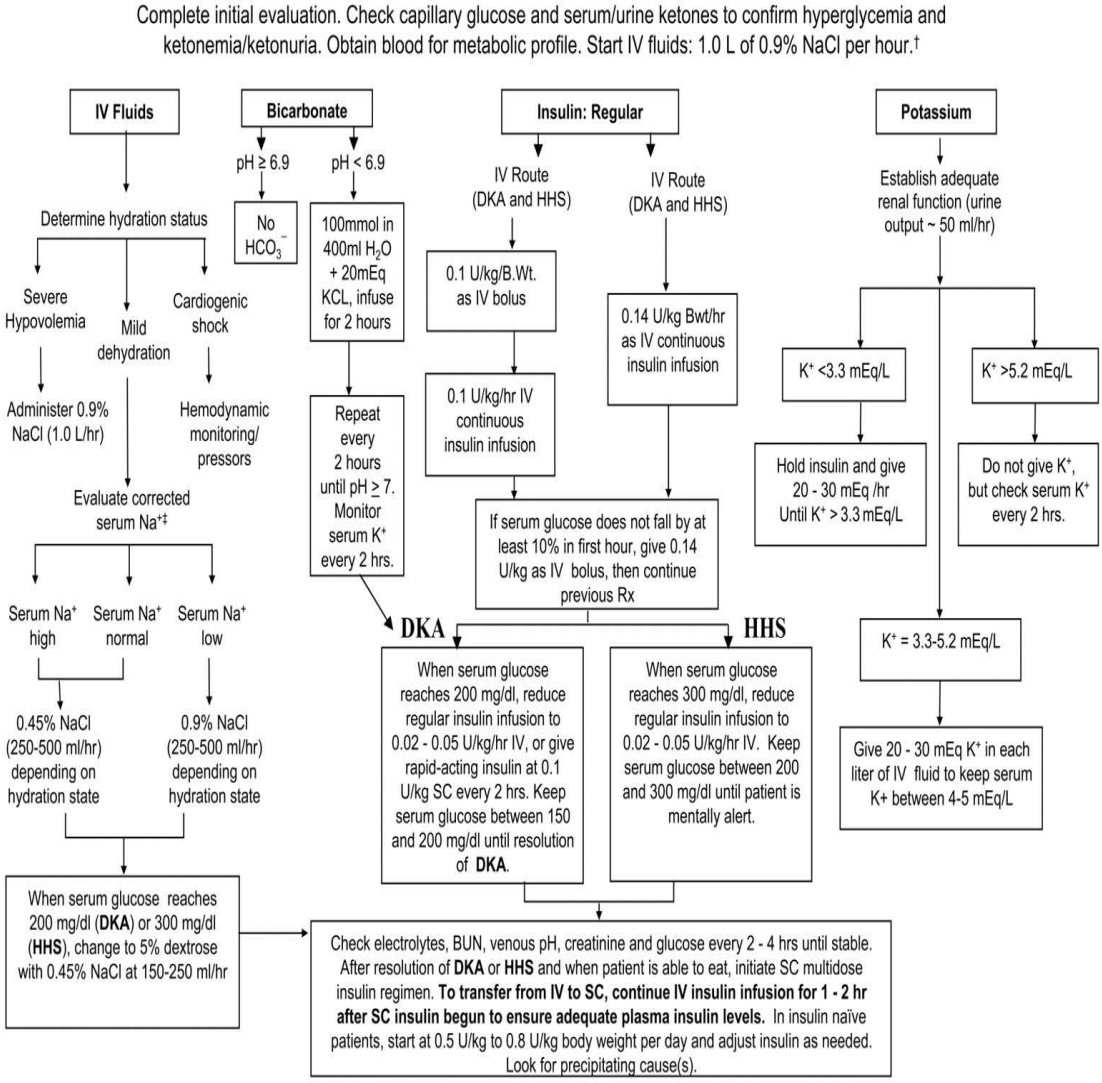


Figure 5 – Treatment of DKA & HHS

Diabetic Retinopathy

It is the most common micro-vascular complications leading to blindness in diabetes. Blindness usually results from diabetic macular oedema, tractional retinal detachment or non-resolving vitreous haemorrhage. Diabetic retinopathy is effectively treatable at early stages when patient is asymptomatic , so annual screening of fundus is mandatory for all diabetic patients.[12]

Modifiable Risk Factors

- Hyperglycemia
- Hypertension
- Dyslipidemia
- Smoking

Non modifiable Risk Factors

- Duration of diabetes
- Age
- Genetic predisposition
- Ethnicity

Pathophysiological Events in Diabetic Retinopathy

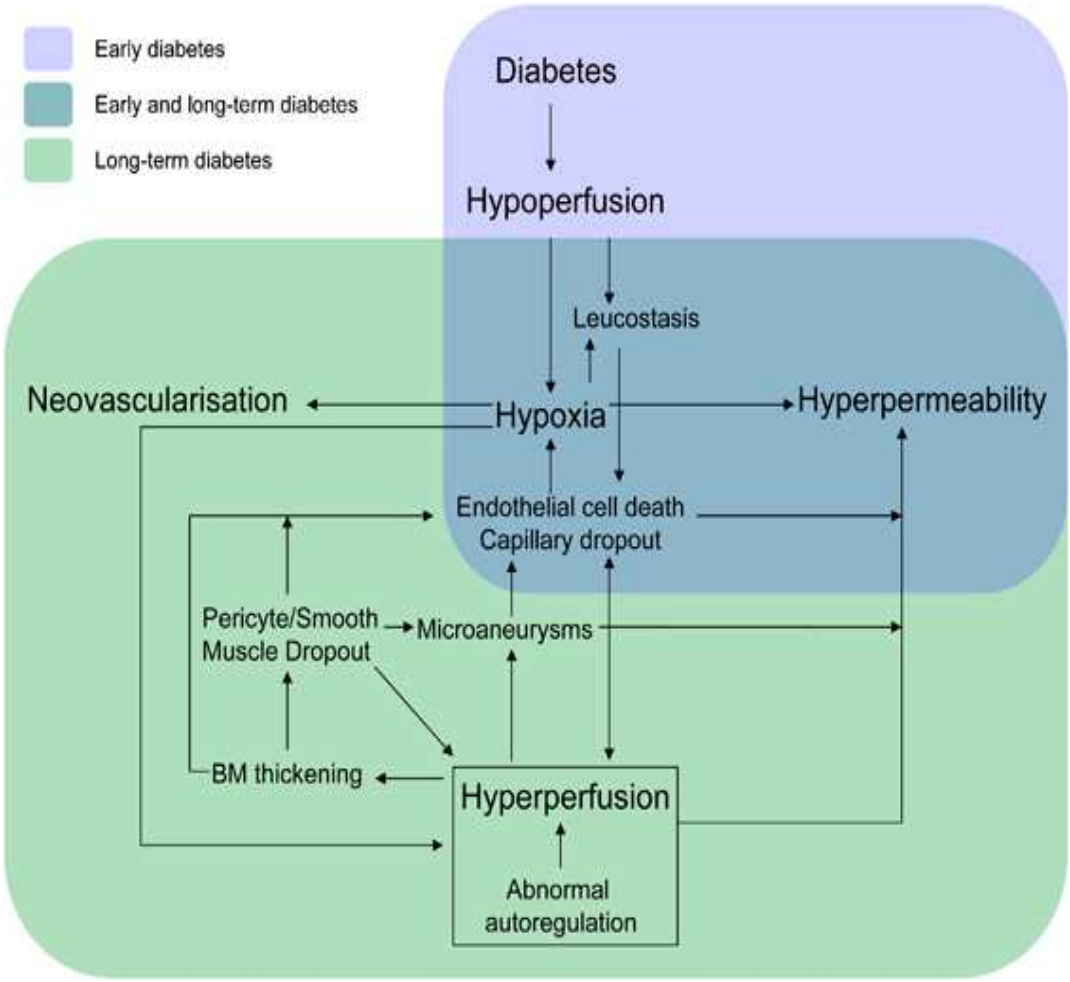


Figure 6 – Pathogenesis of Diabetic Retinopathy

Microangiopathy with vascular occlusion and leakage are the hallmarks of diabetic retinopathy .chronic hypoxia leads to release of vascular endothelial growth factor and formation of new blood vessels leading to proliferative retinopathy.

Spots or floaters, blurred vision , fluctuating vision , impaired color vision, dark or empty areas, vision loss , frequently changing glasses are the clinical manifestation of diabetic retinopathy.

Table 8 – Diabetic retinopathy Classification

RETINOPATHY STAGE	FINDINGS ON OPHTHALMOSCOPY
No apparent retinopathy	No abnormalities
Mild non-proliferative DR (NPDR)	Microaneurysms only
Moderate NPDR	More than just microaneurysms but less than severe NPDR
Severe NPDR	Any of the following: 1. More than 20 intraretinal haemorrhages in each of 4 quadrants 2. Definite venous beading in 2 or more quadrants 3. Prominent intraretinal microvascular abnormalities in 1 or more quadrants AND no signs of proliferative retinopathy
Proliferative DR (PDR)	One of the following: 1. Neovascularisation 2. Vitreous/preretinal haemorrhage
Advanced Diabetic Eye Disease (ADED)	One of the following: 1. Formation of fibrovascular tissue proliferation 2. Traction retinal detachment due to formation of posterior vitreous detachment 3. Dragging of retinal/distortion 4. Rhegmatogenous retinal detachment

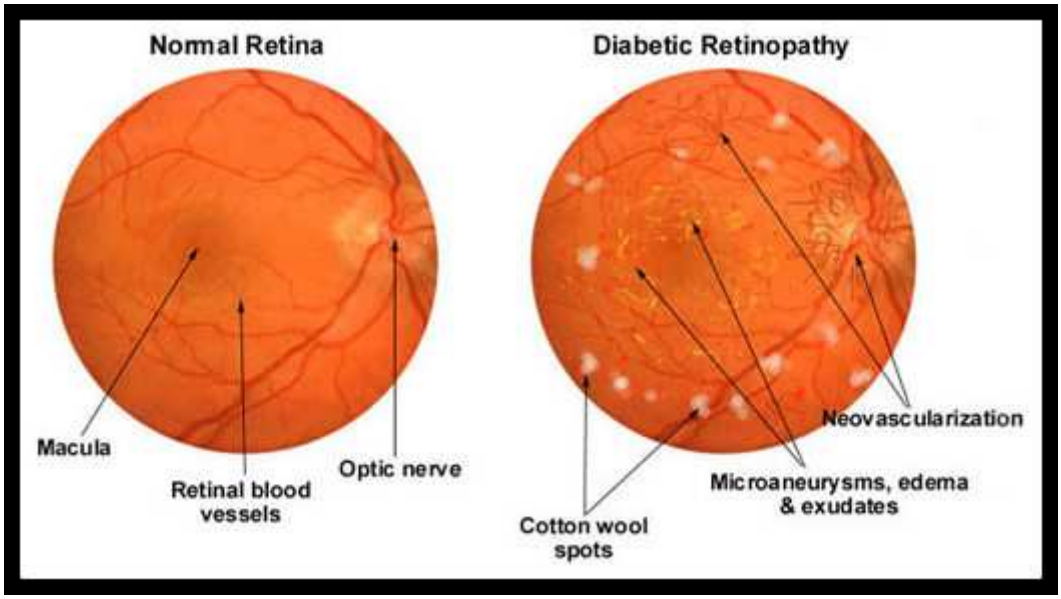


Figure 7 – Fundus of Normal & Diabetic retinopathy

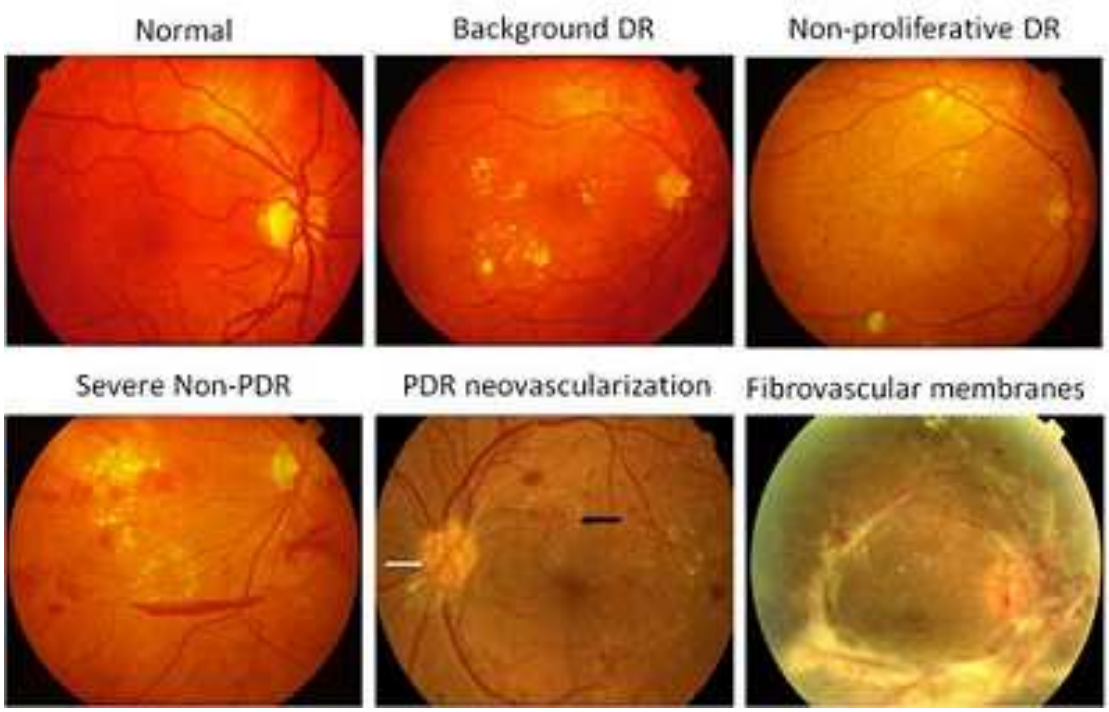


Figure 8 – Fundus of various stages of Diabetic retinopathy

Complications of diabetic retinopathy

1.Vitreous haemorrhage

2.Tractional retinal detachment.

3.Rubeosisiridis and

4.Neovascular glaucoma.

Digital colour retinal photography, fundus fluorescinangiography, perimetry, ultrasound B scan, and optimal coherence tomography are the investigatons available for diabetic retinopathy. Screening of fundus is done by opthalmoscope.

Treatment

Laser photocoagulation

Vitrectomy

Intravitreal injections of anti-VEGF like Bevacizumab.

Diabetic nephropathy

Diabetes is the most common cause of CKD in adults. Proteinuria is the hallmark of diabetic nephropathy. Domenico Cotugno was first to describe proteinuria in diabetes. Patient gradually develops decline in

GFR accompanied by rise in blood pressure and urinary albumin excretion.

It is defined by persistent albuminuria (> 300 mg/day) on at least two occasions separated by 3-6 months[13]

Carl Erik Mogensen classification

1. Stage of renal hypertrophy and glomerular hyperfiltration .
2. Stage of apparent normalcy : clinically silent and last for 5 – 15 years
3. Stage of incipient nephropathy: microalbuminuria and reversible with tratment
4. Stage of overt nephropathy: macroalbuminuria, nephrotic syndrome hypertension and decline in GFR occurs; this stage is irreversible.
5. End stage renal disease: GFR < 15 ml/min , requires renal replacement therapy.

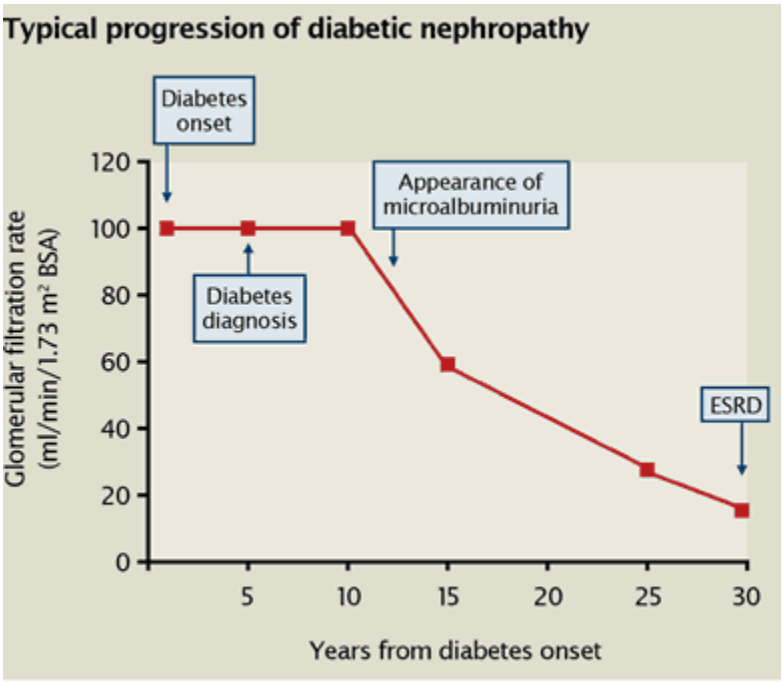


Figure 9 – Diabetic nephropathy Natural course

Screening

All type 2 DM at the time of diagnosis and then yearly, after 5 years onset of type 1 DM and then yearly. Screening of diabetic nephropathy is done by urine examination .spot albumin to creatinine ratio, 24 hr protein collection , timed urine collection are the tests available for screening.

Treatment

DCCT (Diabetes Control and Complications Trial) has shown strict glycemic control (HbA1C <7) reduce the risk of developing microalbuminuria and also slow the progression of microalbuminuria to

overt nephropathy. ACE inhibitors or ARB either one drug can be used to prevent microalbuminuria or reduce the severity of macroalbuminuria.[14]

. Hypertension which is usually present at stage 4 should be managed effectively and target is 125/75 mmHg. In absence of proteinuria BP goal is 130/80. Coronary vascular disease is the common cause of death in diabetic nephropathy. So dyslipidemia needs to be treated with statins.

Diabetic neuropathy

It is characterised by damage to nerve leading to loss of sensation , ulceration and subsequent amputation. It occurs as a result of microangiopathy, symptomatic and asymptomatic neuropathy develop in DM gradually due to hyperglypacemia and hypoinsulinemia.

Pathogenesis

1. Metabolic hypothesis - persistent hyperglycemia, alteration of sorbitol pathway , production of glycosylated end products, oxidative nerve damage.
2. Immune hypothesis – autoantibodies to gangliosides , immune mediated nerve damage.
3. Microvascular hypothesis –impaired vasoconstriction and vasodilation leading to nerve ischemia.

4. Neurotrophic hypothesis – nerve growth factor, neurotrophin 4/5 are deficient in diabetes.
5. Oxidative stress hypothesis – increased free radical formation in diabetes.

Pathogenesis

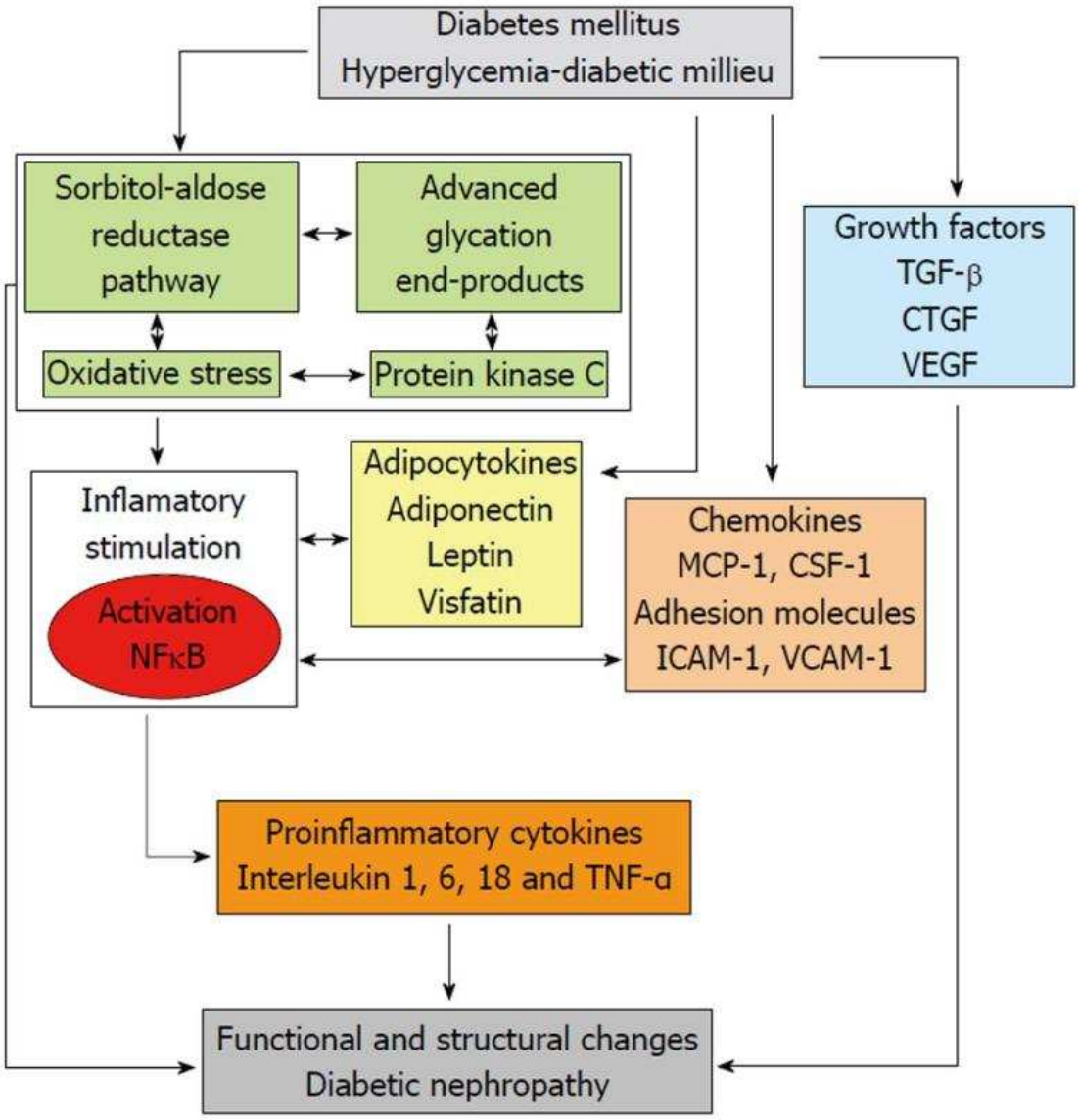


Figure 10 – Pathogenesis of Diabetic neuropathy

Classification

Box 1. Diabetic neuropathies and the subset of painful diabetic neuropathies

General diabetic neuropathies

Symmetric polyneuropathies:

- Acute sensorimotor polyneuropathy[a]
  Chronic sensorimotor polyneuropathy[a]
  Autonomic polyneuropathy[a]

Mononeuropathies:

- Cranial nerves III, VI, VII (ischemic)
- Thoracoabdominal
  Focal limb (*ex*-femoral)
  Proximal motor (amyotrophy)
- Inflammatory demyelinating

Painful diabetic neuropathies

Acute painful neuropathies:

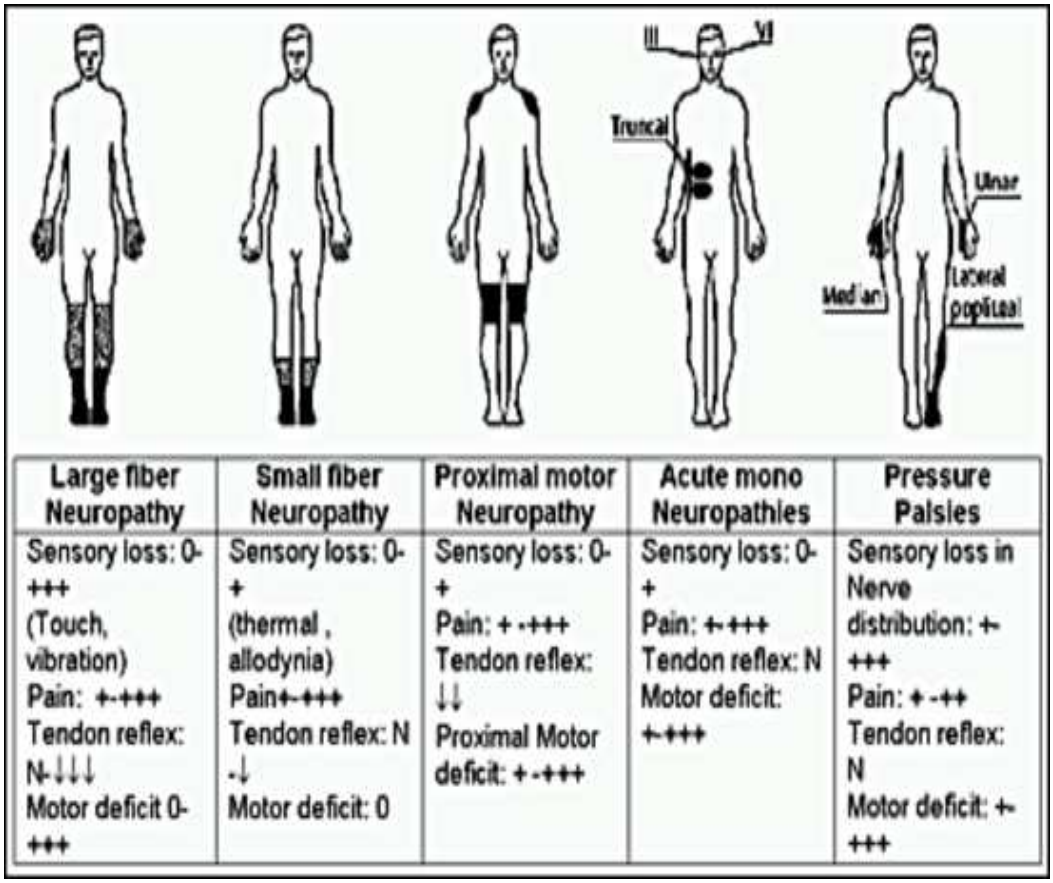
- Distal sensory[a]
- Thoracic radiculopathy (ischemic)
- Lumbar nerve root/plexus (ischemic)
- Insulin neuritis

Chronic painful neuropathies:

- Small fiber distal[a]
- Large fiber distal[a]
- Compressive mononeuropathies[a]
  Carpal tunnel
  Ulnar (cubital tunnel)
  Common peroneal nerve[a]
- Proximal inflammatory demyelinating

[a] Neuropathy most frequently presenting to foot & ankle providers.

Figure 11- Classification of Diabetic neuropathy



Large fiber Neuropathy	Small fiber Neuropathy	Proximal motor Neuropathy	Acute mono Neuropathies	Pressure Palsies
Sensory loss: 0-+++ (Touch, vibration) Pain: +-+++ Tendon reflex: N-↓↓↓ Motor deficit 0-+++	Sensory loss: 0-+ (thermal , allodynia) Pain+-+++ Tendon reflex: N -↓ Motor deficit: 0	Sensory loss: 0-+ Pain: + -+++ Tendon reflex: ↓↓ Proximal Motor deficit: + -+++	Sensory loss: 0-+ Pain: +-+++ Tendon reflex: N Motor deficit: +-+++	Sensory loss in Nerve distribution: +-+++ Pain: + -++ Tendon reflex: N Motor deficit: +-+++

Figure 12 – Diabetic neuropathy Presentation

Macrovascular complications

Cardiovascular disease

Diabetes have two to four field increase for coronary heart disease and heart failure when compared to non diabetes .Coronary heart disease is the common cause of death in diabetes[15]. Both systolic and diastolic heart failure occur in diabetes. In diabetes , heart failure occur due to multiple factors like ischemia , metabolic and functional myocardial derangements.

Screening

1. Resting ECG.
2. Exercise ECG.
3. Stress myocardial perfusion imaging.
4. Stress echocardiography.
5. Cardiac computed tomography
6. Cardiac MRI
7. Angiogram

Screening of cardiovascular disease in diabetes can be done by above test. Choice of screening is based on patient symptoms, cost, availability.

Obesity

Obesity is result of imbalance between higher energy intake and lower energy expenditure in the background of genetic susceptibility.

Parameters used to measure obesity

1. Body mass index
2. Waist circumference
3. Waist – hip ratio
4. Body fat percentage

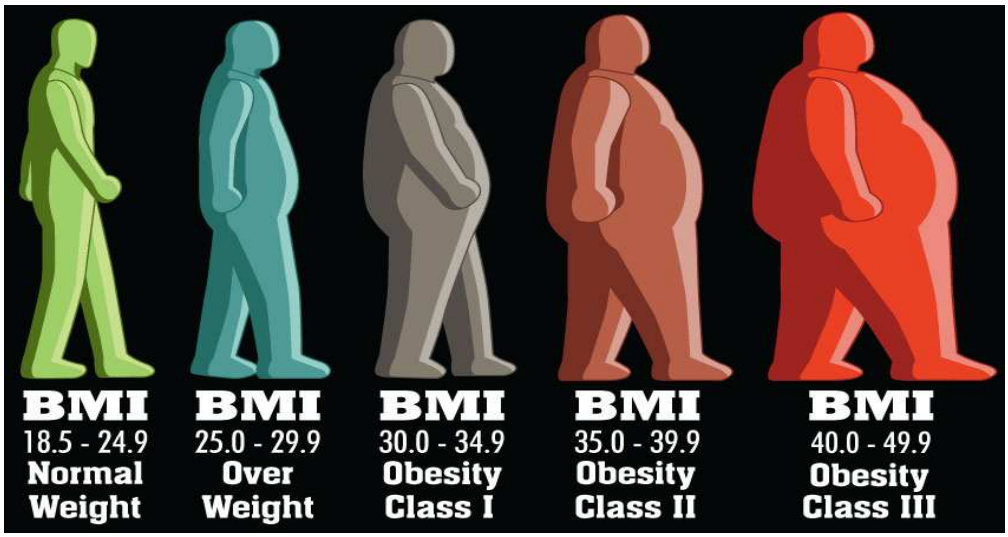


Figure 13 – Obesity classification

Body mass index = weight (kg)/ height ^{2}(m). BMI > 23 is overweight and > 25 is obese in indian population.

Figure 14 – Medical problems in Obesity

ZINC

Zinc is an essential trace element. Before discovery of zinc as a metal, it is used as zinc salts for medical purposes. Persians used zinc vitriol solution to treat eye inflammation. In india metallic zinc was produced around 1200 AD. Copper – zinc alloy brass was found in literature around 1400 – 1000 BC[16]

Zinc metabolism

Dietary zinc is absorbed in small intestine. Phytates and iron inhibits absorption of zinc. Normal value of zinc in blood is in the range of 70 – 120 microgram/dl. 60% bound to albumin and 30% bound to macroglobulin .zinc is mostly stored intracellularly and bound to metalloproteins. Zinc is primarily stored in liver and kidney.

Functions of zinc

1. Zinc is co factor for more than 70 enzyme systems which includes dehydrogenases, carbonic anhydrase, carboxypeptidase and alkaline phosphatase.

2. Regulates nucleoproteins and plays important role in growth, tissue repair and wound healing.

3. It plays a role in insulin storage and secretion and involved in carbohydrate metabolism.

4. Zinc plays a role in immune function .its deficiency is associated with infection. Zinc has inhibitory effect on cholera toxin and E. coli heat labile toxin.

5. It plays a role in testicular harmone synthesis and gonadal function.

Recommended dietary allowance for adult is 11mg/day and children is 8 mg/day. Dietary sources of zinc include animal products, milk, egg, nuts , legumes and cereals.

Zinc deficiency

1.Severe growth retardation.

2. Frequent infections especially diarrhoea and pneumonia.

3. Hypogonadism.

4. Anemia.

5. Bullous pustular dermatitis , rough skin.

6. Alopecia.

7. Impaired taste and smell.

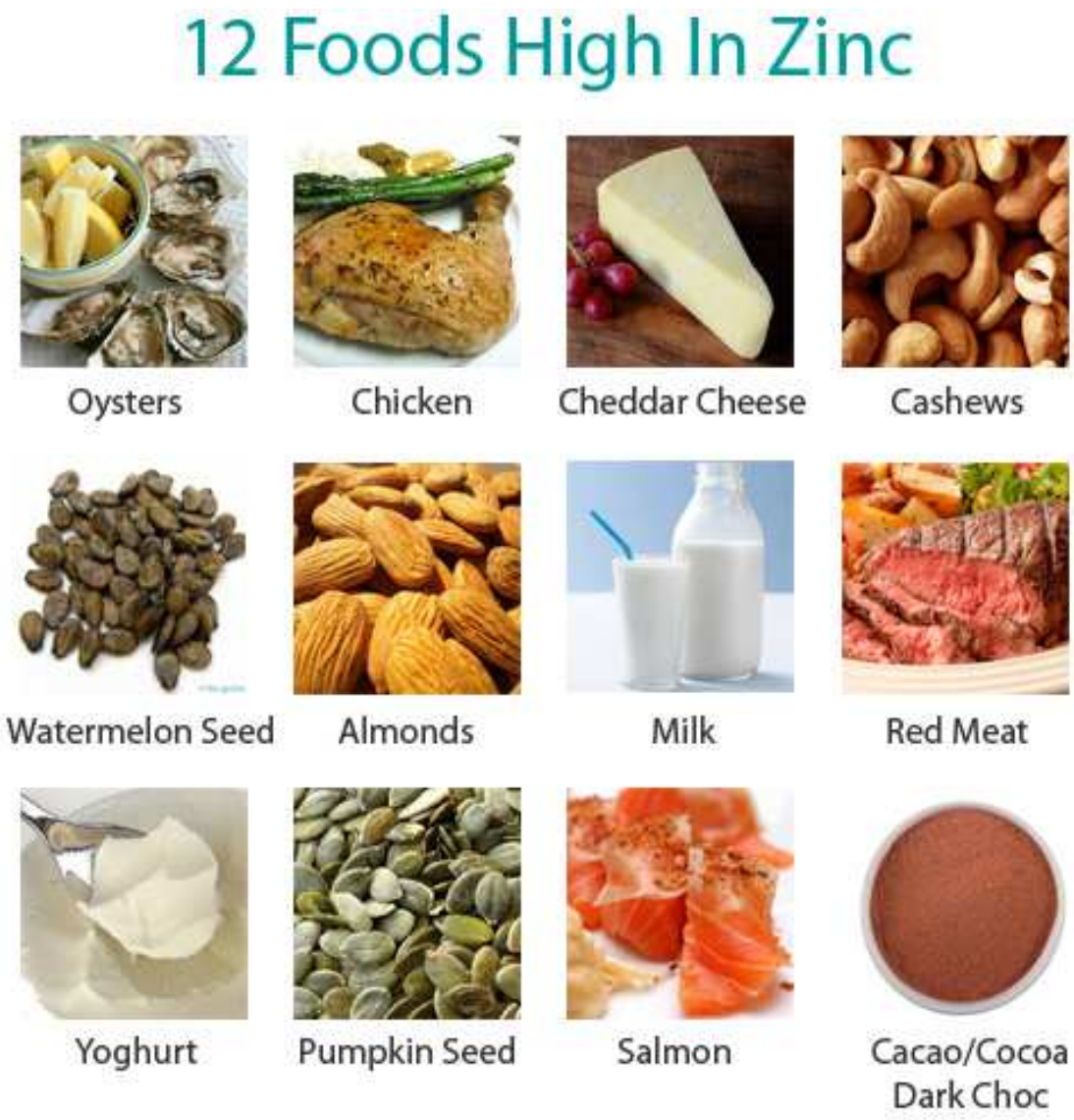


Figure 14 – Zinc rich foods

Pancreas and zinc

Pancreas is both an exocrine and endocrine organ . It secretes insulin and glucagon which plays important role in maintaining blood glucose in normal range.Pancreas also secretes trypsin , amylase and lipase which plays a role in protein , carbohydrate and lipid metabolism respectively.so zinc deficiency alter pancreas endocrine metabolism and affect glycemic status.

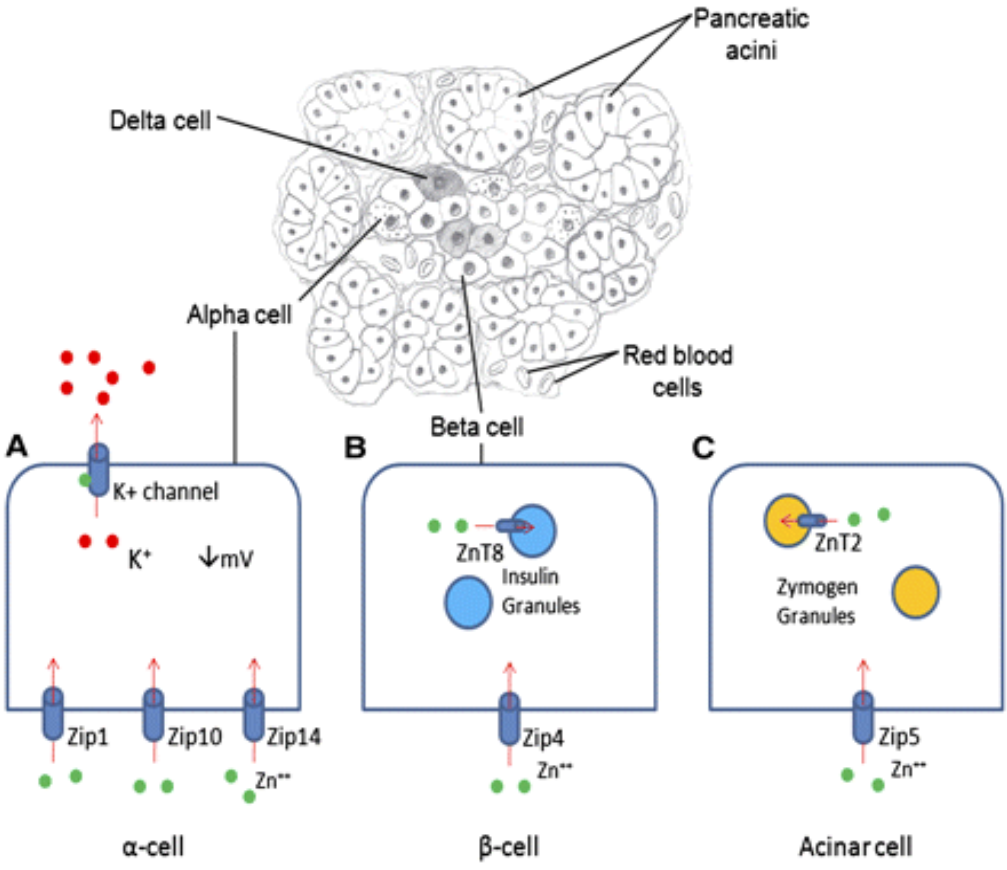


Figure 16 – Zinc transport in Pancreas

(A) Zip1, Zip10, Zip 14 are located in alpha pancreatic cell and plays a role in zinc transport into pancreatic cell. Zinc after binds with ATP dependent potassium channel and and efflux and inactivates voltage dependant calcium channel and decrease glucagon secretion in alpha cell.

(B) Zip4 involves in transport of zinc into beta pancreatic cell and then ZnT8 helps zinc entering into insulin granules .zinc helps in secretion of insulin from beta pancreatic cell.

(C) Zip5 helps zinc transports into pancreatic acinar cell and then it enters zymogen granules with the help of ZnT2 . Trypsin, amylase and lipase are secreted with the help of zinc from zymogen granules.

Zinc and Diabetes mellitus

Zinc dysregulation is associated with both type 1 and type 2 DM. Zinc deficiency is associated with decrease insulin release from pancreas and hyperglycemia .

Zinc deficiency is associated with decreased insulin sensitivity in rat offspring. Its deficiency is also associated with weight gain in rat offspring. Severe zinc deficiency is associated with hyperglycemia and hyperinsulinemia and implicating zinc role in glucose regulation[17]Apart from zinc , zinc transporter (ZnT8) is also implicated in pathogenesis of diabetes mellitus. ZnT8 helps zinc enter into insulin granules and then

insulin secretion. In animal study ZnT8 knock out mice becomes glucose intolerant after eating high fat diet indicating under physiological stressful condition (eg obesity) ZnT8 is essential for glucose control.

Antibodies formed against ZnT8 is associated with diabetes mellitus. these antibodies are seen in 60 to 70% of newly diagnosed type 1 DM. this indicates ZnT8 dysfunction is associated with impaired glucose control.

Zinc supplementation (Zn(11)-thioallixin-N-methyl) given to mouse model of type 2 DM is associated with lowered blood glucose. In another study mice were given zinc enriched water for 1 week before administering streptozotocin and these mice were from streptozotocin induced diabetes.

Zinc increases metallothionen level in pancreas and scavenges free radicals in pancreas .this protects beta cell from destruction and maintains insulin homeostasis. Thus zinc therapy may be beneficial in Diabetes mellitus.

Oxidative stress and Zinc

In diabetes, oxidative stress damage to cell is the end result of both microvascular and macrovasular complications. Zinc and copper are anti

oxidants. Zinc due to its antioxidant property decreases both micro and macrovascular complication in diabetes.

Metallothionein is cysteine rich compound which has active site for zinc. It scavenges free radicals which is responsible for oxidative damage to cell. Zinc is an integral part of metallothionein and induces it.

Hyperglycemia increases Reactive oxygen species (ROS) which causes cell damage .Metallothioneinrelease zinc in response to increased ROS .this released zinc antagonise redox active transition metals like iron and copper which is responsible for formation of hydroxide and superoxide radicals.[18]

. Zinc also inhibits NADPH oxidase and also it forms integral component of Cu/Zn superoxide dismutase which converts superoxide to hydrogen peroxide .hydrogen peroxide is then converted to water by glutathione zinc.

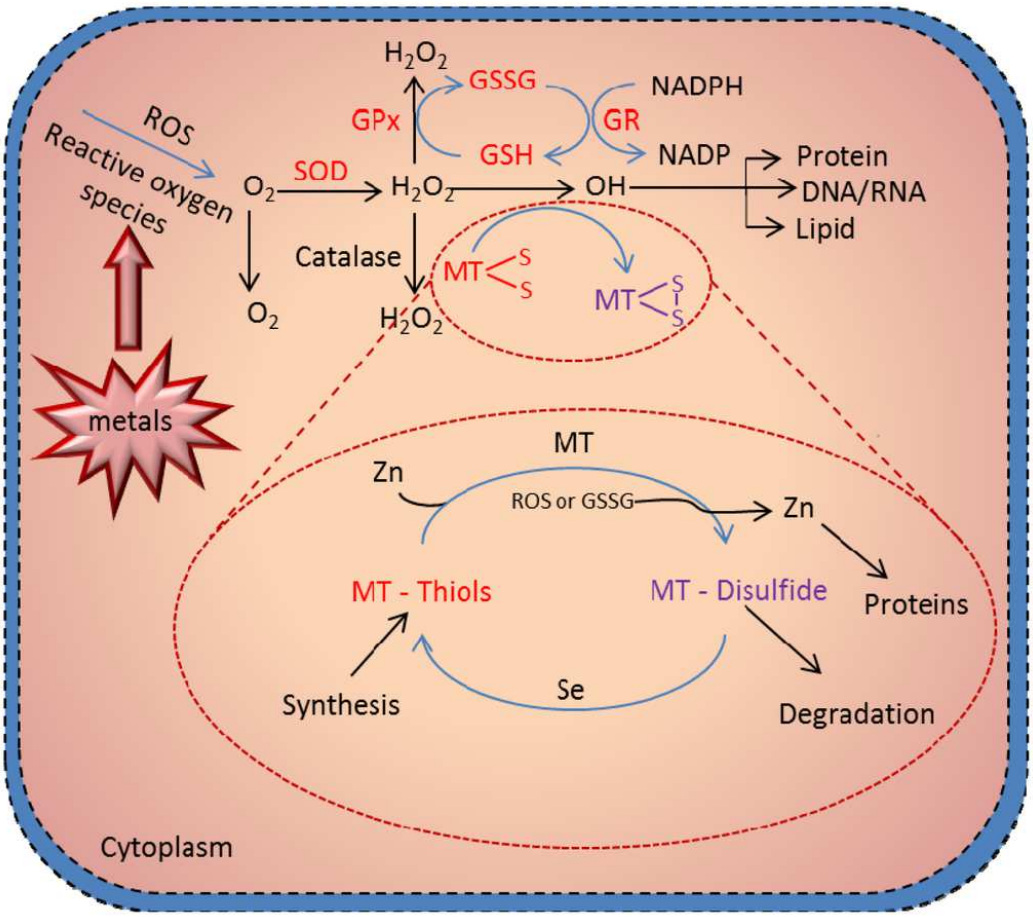


Figure 17 – Antioxidant mechanism of Zinc

Zinc and Hypertension

Hypertension is defined as blood pressure > 140/90. Zinc deficiency cause taste impairment which leads to high salt intake[19]Excess sodium causes water retention and increases blood pressure.

Many enzymes like nitric oxide synthase and angiotensinogen converting enzyme that regulate blood pressure contain zinc in their structure .nitric oxide produced by endothelial cells plays a role in maintaining arterial blood flow and pressure. Zinc is present in nitric oxide synthase in the form of zinc thiolate which its active catalytic site.[20]

Zinc by its antioxidant property decrease oxidative stress to vascular endothelium .Zinc deficiency can disrupt endothelial cell function and increases oxidative damage .blood pressure rise in zinc deficiency depends on age and duration of zinc deficient.

Superoxide ion inactivates nitric oxide produced produced from endothelium and leads to vasoconstriction and increase in blood pressure. Zinc by its antioxidant property decreases superoxide ion and increase nitric oxide production and maintains blood pressure.

Zinc and Obesity

Zinc role in obesity remains unclear. In some studies high leptin level in obesity is associated with decreased zinc level in body .in one study obese patients with low zinc status have normalised zinc level following low caloric diet.

Zinc and Dyslipidemia

Triglyceride and cholesterol levels are high in zinc deficient individual in some studies . exact mechanism is unknown. HDL cholesterols increases with zinc supplementation in some studies .

Zinc and Cardiovascular

Zinc supplementation decrease cardiovascular mortality by controlling blood glucose, preventing vessel damage by antioxidant property and improving HDL cholesterol.

HbA1c(Glycated haemoglobin)

Glycation is a addition of glucose residue to amino group of protein. Plasma proteins, haemoglobin , membrane and lens protein undergo glycosylation in our body. Among all these proteins glycosylation of haemoglobin forms major fraction around 80%.

HbA1c serve as a good indicator of plasma glucose level over past 3 months. It should be performed at the time of diagnosis and then every 3 months to assess control of diabetes.

Table 9 - HbA1c and mean plasma glucose level

A1C	Estimated Average Glucose (eAG)
12%	298 mg/dL
11.5%	283 mg/dL
11%	269 mg/dL
10.5%	255 mg/dL
10%	240 mg/dL
9.5%	226 mg/dL
9%	212 mg/dL
8.5%	197 mg/dL
8%	183 mg/dL
7.5%	169 mg/dL
7%	154 mg/dL
6.5%	140 mg/dL
6%	126 mg/dL
5.5%	111 mg/dL
5%	97 mg/dL

1. Nondiabetic range 4.5 – 5.8%
2. Prediabetic range 5.8 – 6.5%
3. Diabetic range > 6.5 %

HbA1c value of less than 4.5 % is associated with serious risk of hypoglycaemia. False values occurs in hemoglobinopathies(thalassemia), anemia and uremia. Zinc deficiency increases blood glucose and increases HbA1c . Fructosamine is another glycated compound which can be used to measure mean glucose level for past 2-3 weeks.

MATERIALS

AND

METHODS

MATERIALS AND METHODS

SETTING

This study was conducted at the Institute of Internal medicine, Rajiv Gandhi Government General Hospital and Madras Medical College.

ETHICAL COMMITTEE APPROVAL

Obtained.

STUDY DURATION

This study was conducted over a period of six months.

STUDY POPULATION

Patients attending Medicine outpatient department at Institute of Internal medicine

SAMPLE SIZE

100 patients , of which 50 are diabetic who attended medicine out patient department and 50 are control who attended master health check up.

DESIGN OF THE STUDY

Cross sectional study.

INCLUSION CRITERIA

1.Confirmed cases of newly diagnosed Type 2 diabetes mellitus in the age group 40 to 60.

2. Control group with no known comorbidities.

3. Patient and control with hypertension and obesity are included in this study.

EXCLUSION CRITERIA

1. Patient who is taking zinc supplementation or drugs that interfere with zinc absorption.
2. Patient with chronic disease and pregnancy.
3. Patient with diabetic related complications.
4. Patient on oral hypoglycemic or insulin.

ANALYSIS PLAN

Statistical analysis was done using SPSS software version 20.0

SPONSORSHIP

No

CONFLICT OF INTEREST

None

DATA COLLECTION AND METHODS

Informed consent was obtained from each patient .

Patients had their history taken according to a Questionnaire and were subjected to clinical examination .

Patients were subjected to investigations like

HbA1c

Fasting plasma glucose

Renal function test

Fasting lipid profile

Electrocardiogram

HISTORY

History includes age ,sex address, occupation ,presenting complaints, past history, personal history, family history and treatment history

GENERAL EXAMINATION

BMI is calculated based on weight and height using the formula weight/height in meter square. Blood pressure, pulse and other findings are noted.

SYSTEMIC EXAMINATION

CARDIOVASCULAR

RESPIRATORY

ABDOMEN

CENTRAL NERVOUS SYSTEM

FUNDUS OF EYE

INVESTIGATIONS

Serum creatinine - Alkaline picrate method.

Serum urea - Modified Berthelot method.

HbA1c - Automated high performance liquid chromatography.

Serum Zinc - End point Nitro PAPS dye binding.

Serum cholesterol –Cholesterol oxidase method.

Serum triglyceride –Glycerolkinase peroxidase method.

Fasting plasma glucose - glucose oxidase / peroxidase method.

Urine PCR: urine proteins determined by turbidimetric method using 3% sulphosalicylic acid.

All the investigation were done at lab of Department of Biochemistry by well trained technicians.

OBSERVATION

AND

RESULTS

OBSERVATION AND RESULTS

Age distribution in diabetes and control

Table 10 – Age distribution

AGE	Diabetes	Control
41-50 years	33	29
51-60 years	17	21
Total	50	50

In our study 100 patients are included in which 50 are diabetic and 50 are contaol. In diabetic 33 people are in the age group 41 to 50 and 17 people are in the age group 51 to 60. In control 29 people are in the age group 41 to 50 and 21 people are in the age group 51 to 60.

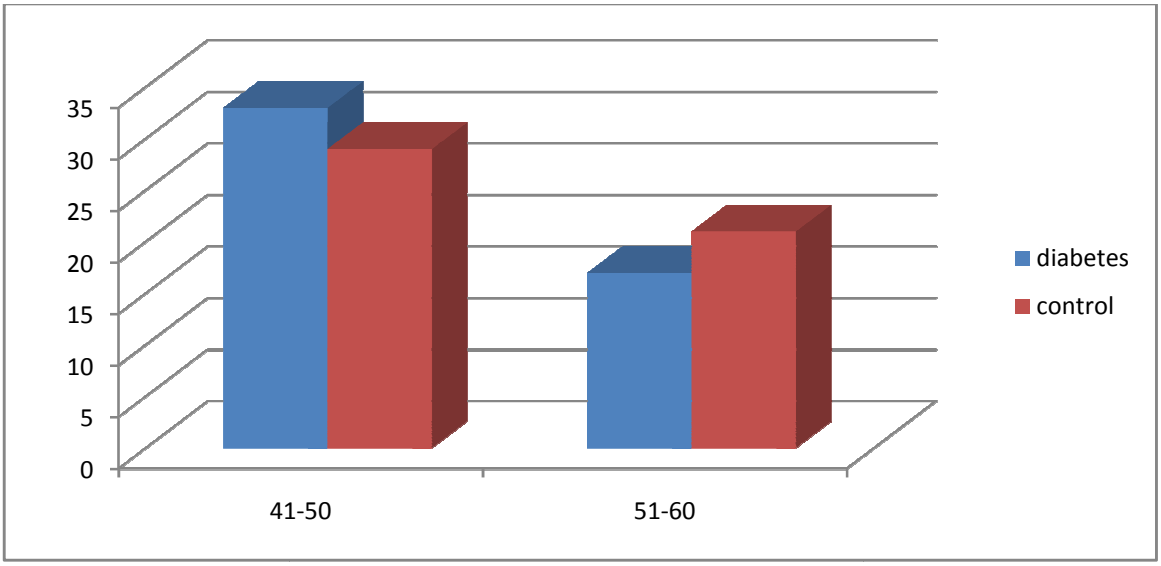


Figure 18 – Age distribution in diabetes and control

Sex distribution in diabetes and control

Table 11 – Sex distribution

SEX	Diabetes	Control
Male	25	23
Female	25	27

In our study 25 people are male and 25 people are female in diabetic group. 23 people are male and 27 people are female in control group.

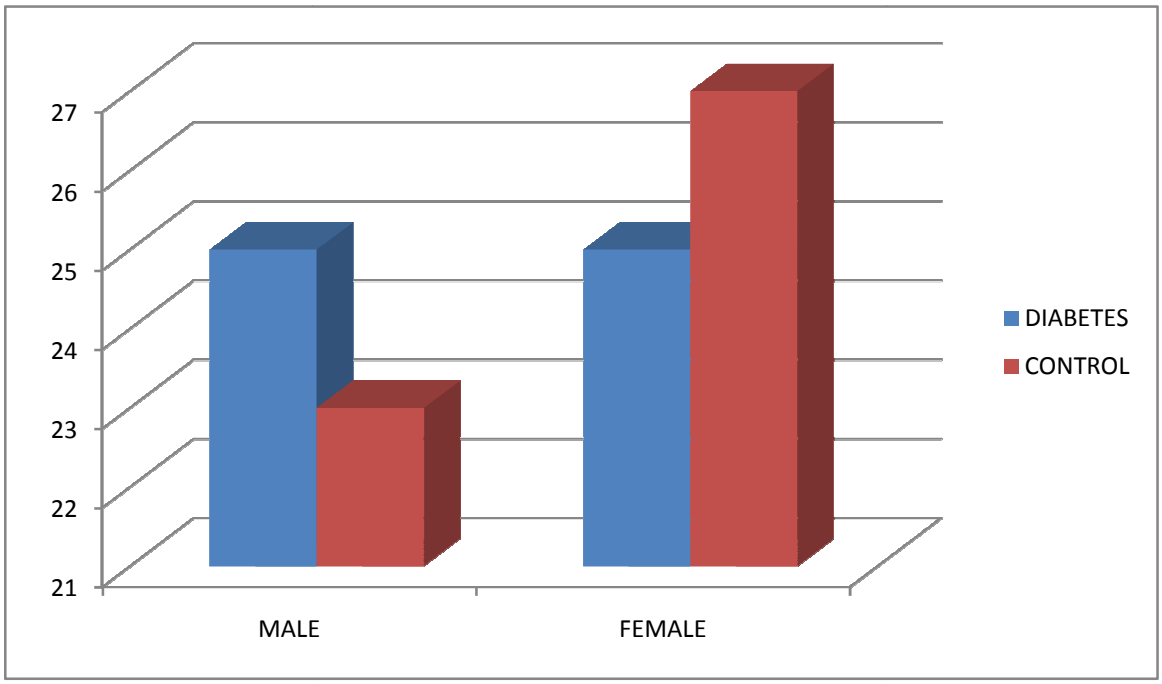


Figure 19 – Sex distribution in diabetes and control

Table 11 - Independent sample t test

	Diabetes		Control		Pvalue
	Mean	**SD**	**Mean**	**SD**	
HbA1C	8.57	1.51	5.41	0.38	<0.001
FBS	189.40	51.14	92.04	12.55	<0.001
Urea	32.90	8.08	30.48	7.90	<0.133
Creatinine	0.82	0.20	0.78	0.20	<0.341
BMI	32.48	3.37	29.35	3.36	<0.001
SBP	132.60	11.97	125.68	11.54	<0.004
DBP	82.52	7.89	79.88	6.76	<0.076
ZINC	58.31	17.23	75.65	18.05	<0.001
Triglyceride	196.58	53.30	173.04	52.27	<0.028
Cholesterol	225.76	51.90	202.96	50.11	<0.028

HbA1c in diabetes and control

Table 12 -Mean and Standard Deviation of HbA1c

	Mean	SD
Diabetes	8.57	1.51
Control	5.41	0.38

In our study mean HbA1c in diabetic and control group are (8.57 ± 1.51) and (5.41 ± 0.38) respectively and it is statistically significant (p value < 0.001).

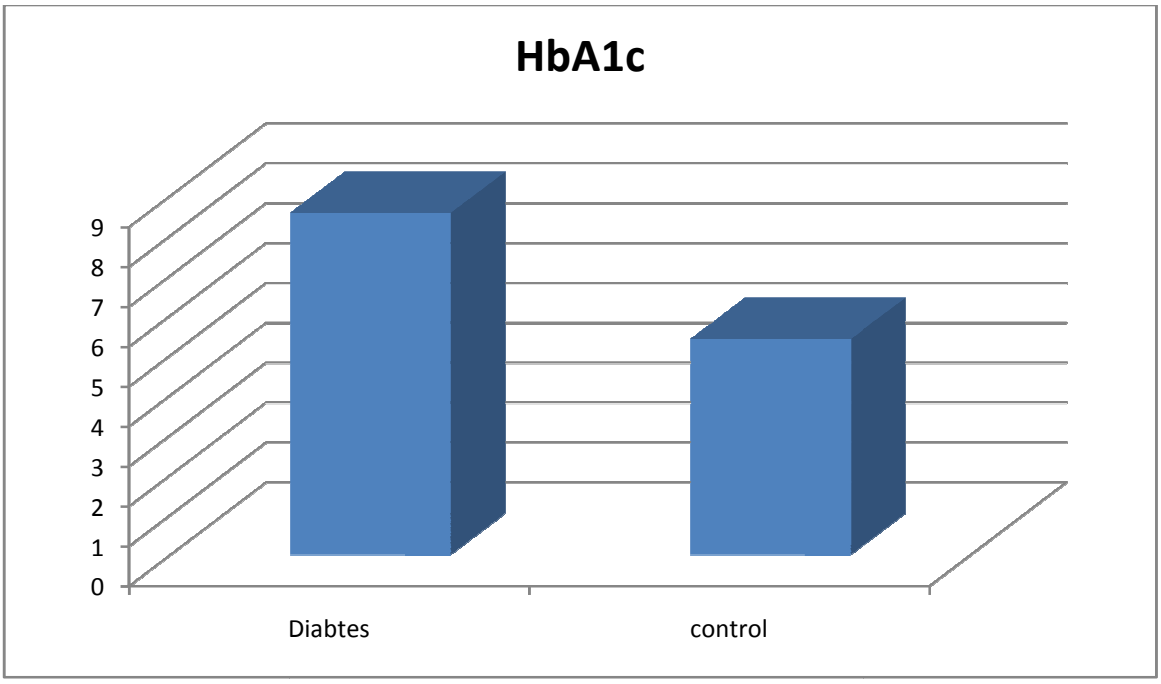


Figure 20 - Mean HbA1c in diabetes and control

Fasting Blood Sugar in diabetes and control

Table 13 – Mean & Standard Deviation of FBS

	Mean	SD
Diabetes	189.40	51.14
Control	92.04	12.55

In our study mean fasting blood sugar in diabetic and control are (189.40 ± 51.14) and (92.04 ± 12.55) respectivelyand it is statistically significant (p value < 0.001).

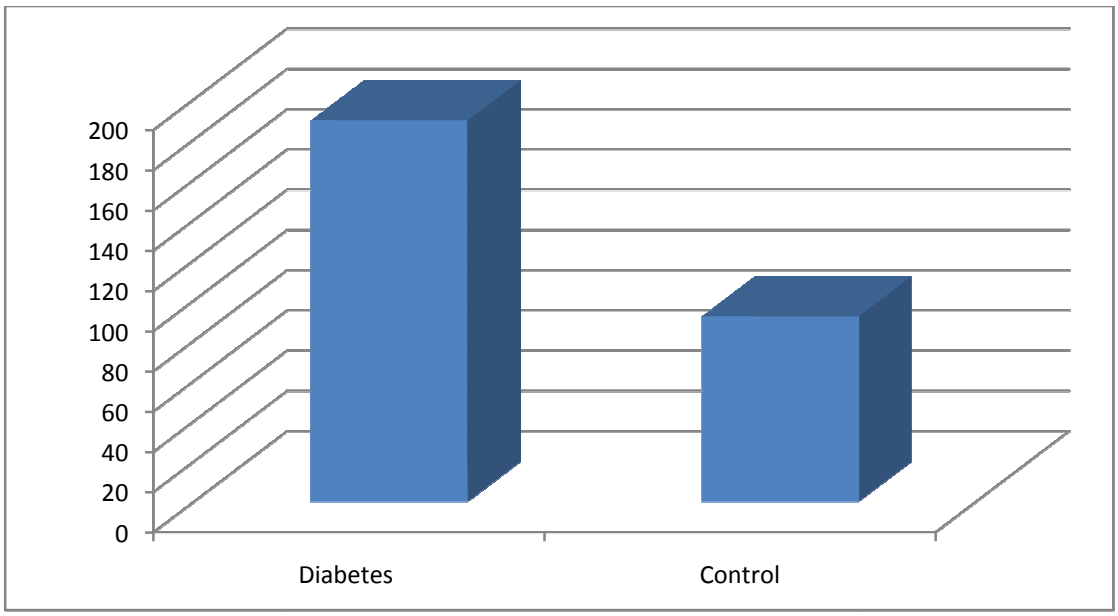


Figure 21 –Mean FBS in diabetes and control

Correlation of Zinc in diabetes and control

Table 14 – Mean and Standard Deviation of Zinc

	Mean	SD
Diabetes	58.31	17.23
Control	75.65	18.05

In our study the mean zinc value in diabetic goup is (58.31± 17.23) which is lower than control group (75.65 ± 18.05) and statistically significant (P value is < 0.001).

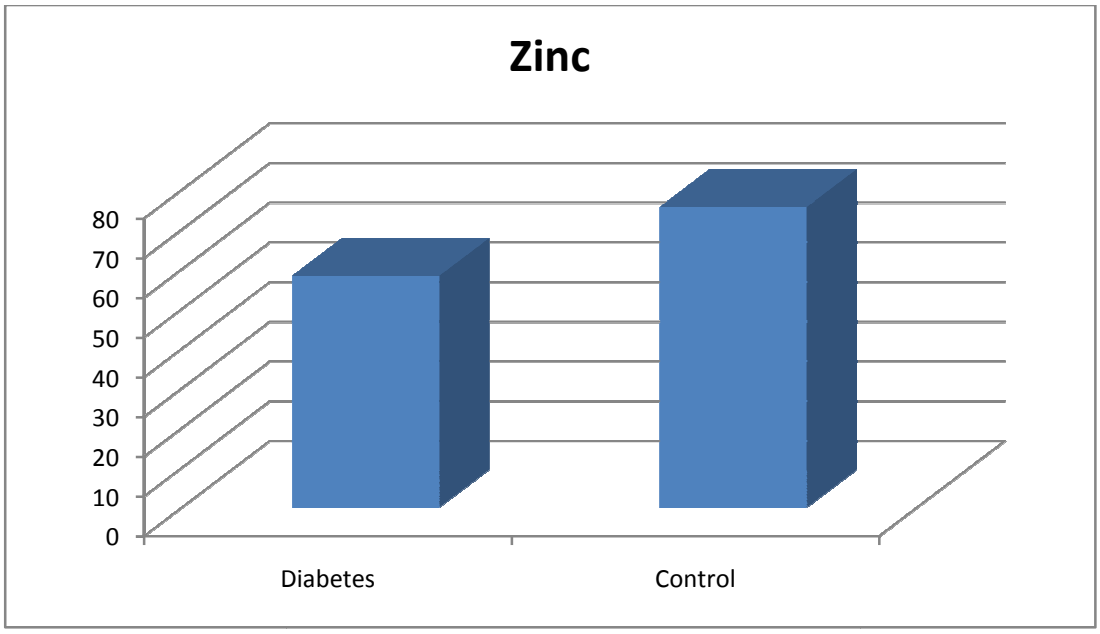


Figure 22 – Mean Zinc value in diabetes and control

Correlation of BMI in diabetic and control group

Table 15 – Mean and Standard Deviation of BMI

	Mean	SD
Diabetes	32.48	3.37
Control	29.35	3.36

In our studythe mean BMI in diabetic group is (32.48 $\pm$ 3.37) which is higher than control group (29.35 $\pm$ 3.36) and statistically significant (p value < 0.001).

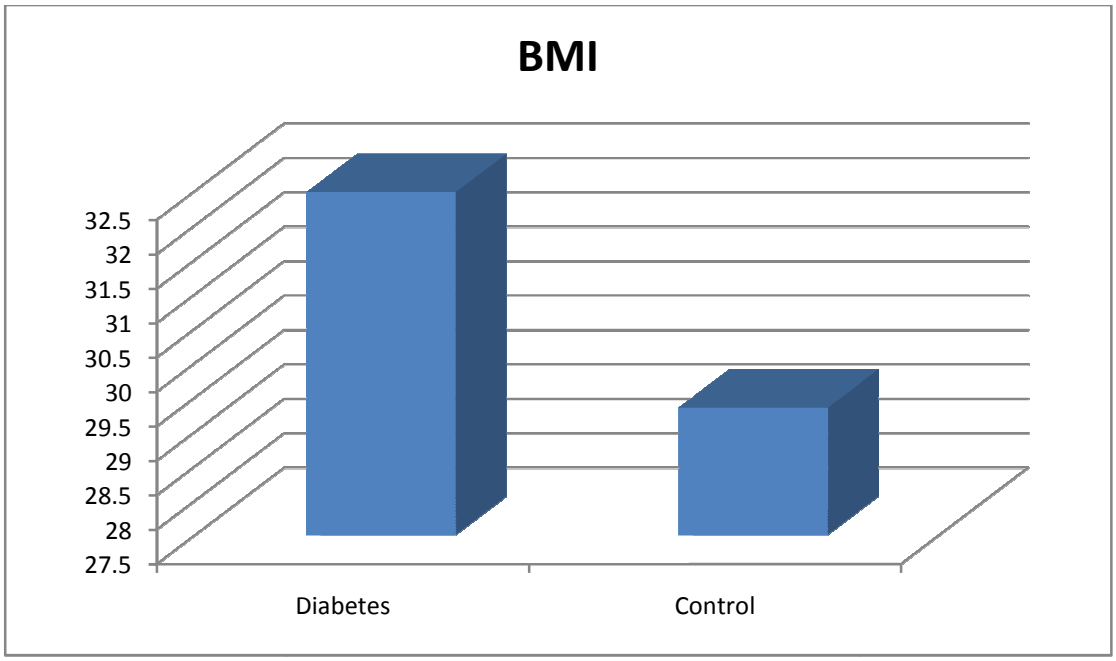


Figure 23 – Mean BMI of diabetes and control

Correlation of Blood pressure in diabetic and control

Table 16 – Mean and Standard Deviation of Blood pressure

	Mean		SD	
	SBP	**DBP**	**SBP**	**DBP**
Diabetes	132.60	82.52	11.97	7.89
Control	125.68	79.88	11.54	6.76

The mean systolic blood pressure (132.60 $\pm$ 11.97) is higher and statistically significant (p value < 0.004)in diabetic group whereas mean diastolic blood pressure is not statistically significant (p value < 0.076).

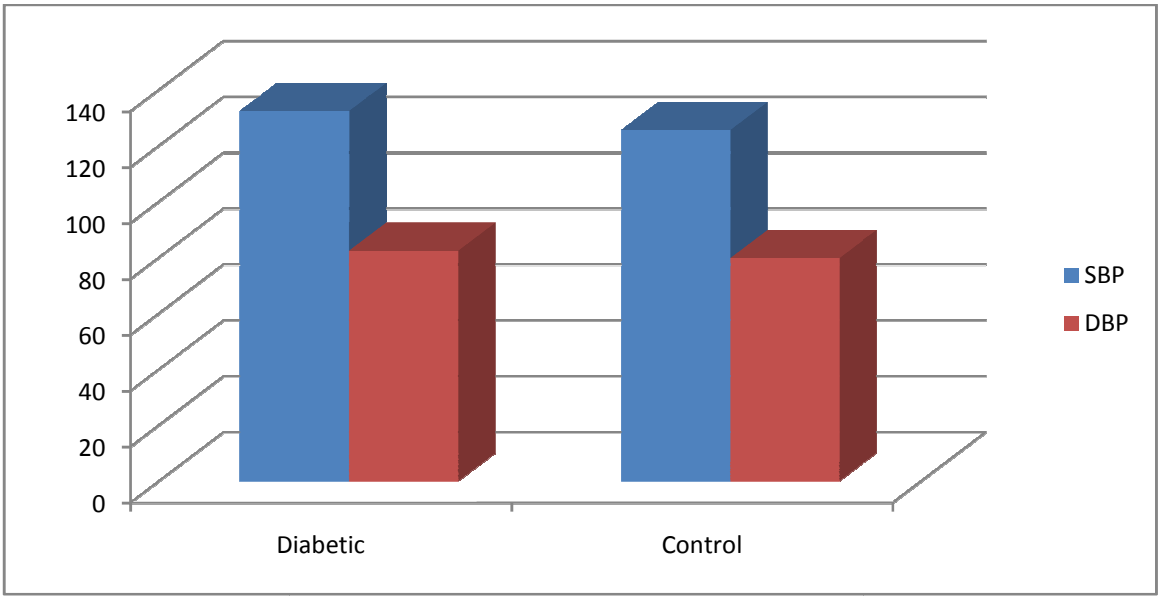


Figure 24 – Mean SBP and DBP of diabetes and control

Correlation of dyslipidemia in diabetic and control

Table 17 – Mean and Standard Deviation of Triglyceride & Cholesterol

	Mean		SD	
	Triglyceride	**Cholesterol**	**Triglyceride**	**Cholesterol**
Diabetes	196.58	225.76	53.30	51.90
Control	173.04	202.96	52.27	50.11

In our study mean cholesterolin diabetic group (225.76± 51.90) is higher than control (202.96 ± 50.11) and statistically significant (p value<0.028). Mean triglyceridein diabetic group(196.58 ± 53.30) is higher than control(173.04 ± 52.27) and statistically significant (p value<0.028).

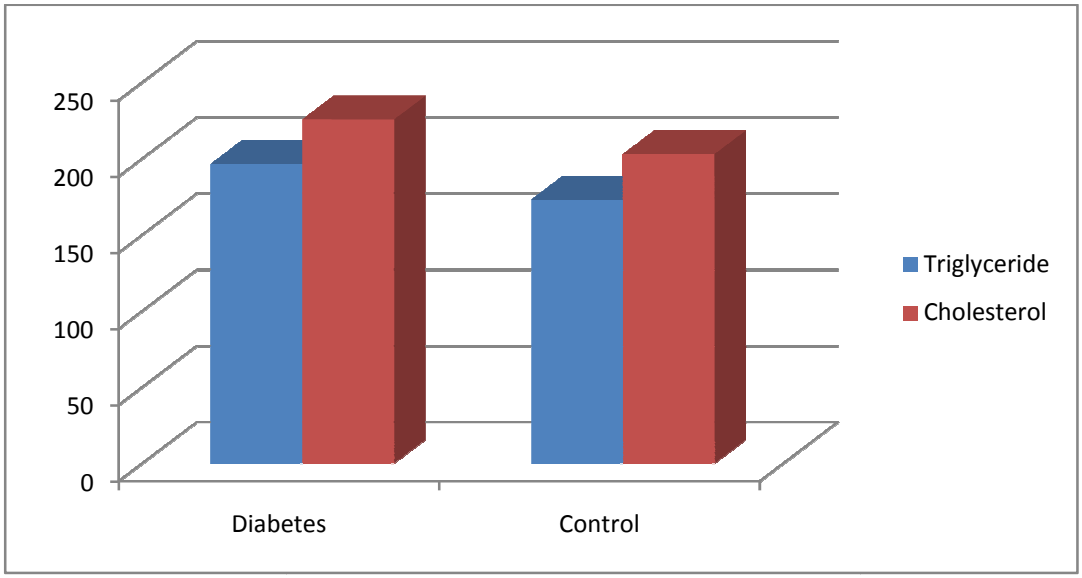


Figure 25 – Mean Triglyceride and Cholesterol in diabetes and control

Table 18 - Correlation of Zinc with various parameters in diabetes and control.

Parameters	Correlation coefficient		P value	
	Diabetes	Control	Diabetes	Control
HbA1c	-0.543	-0.120	<0.001	<0.408
Fasting blood sugar	-0.553	-0.084	<0.001	<0.563
Body mass index	-0.492	-0.161	<0.001	<0.264
Systolic blood pressure	-0.351	-0.103	<0.012	<0.477
Diastolic blood pressure	-0.422	-0.146	<0.02	<0.311
Triglyceride	-0.451	-0.045	<0.001	<0.756
Cholesterol	-0.422	-0.046	<0.001	<0.749

Correlation of Zinc with HbA1c in diabetes

Table 19 – HbA1c and Zinc correlation

HbA1c	No of diabetes	Mean Zinc value
<8	24	60.27
8 – 10	20	55.80
>10	6	39.30

In our study diabetes is divided into three groups based on HbA1c . Mean zinc value decreases with increase in HbA1c and statistically significant (p value <0.001). Pearson correlation coefficient for zinc and HbA1c in diabetes and control are -0.543 and -0.120 respectively and correlation is higher for diabetes than control.

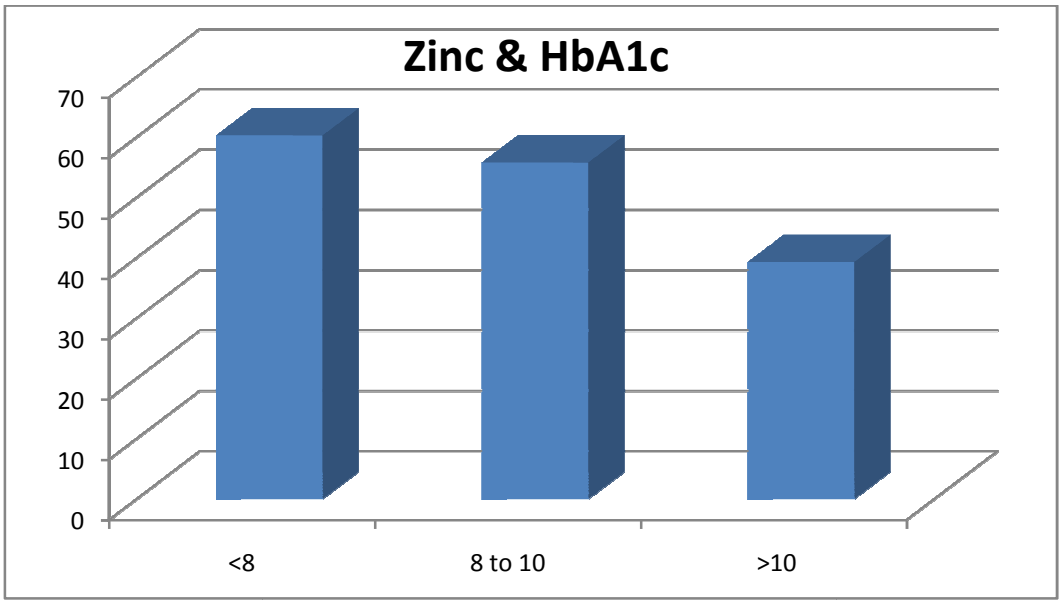


Figure 26 – HbA1c and Zinc correlation

Correlation of zinc and FBS in diabetes

Table 20 – FBS & Zinc correlation

FBS	No of diabetes	Mean zinc value
≤200	26	66.65
201-300	18	53.8
>300	6	40.8

Mean zinc value decreases with increase in FBS and statistically significant (p value <0.001). Pearson correlation coefficient for zinc and FBS in diabetes and control are -0.553 and -0.084 respectively and correlation is higher for diabetes than control.

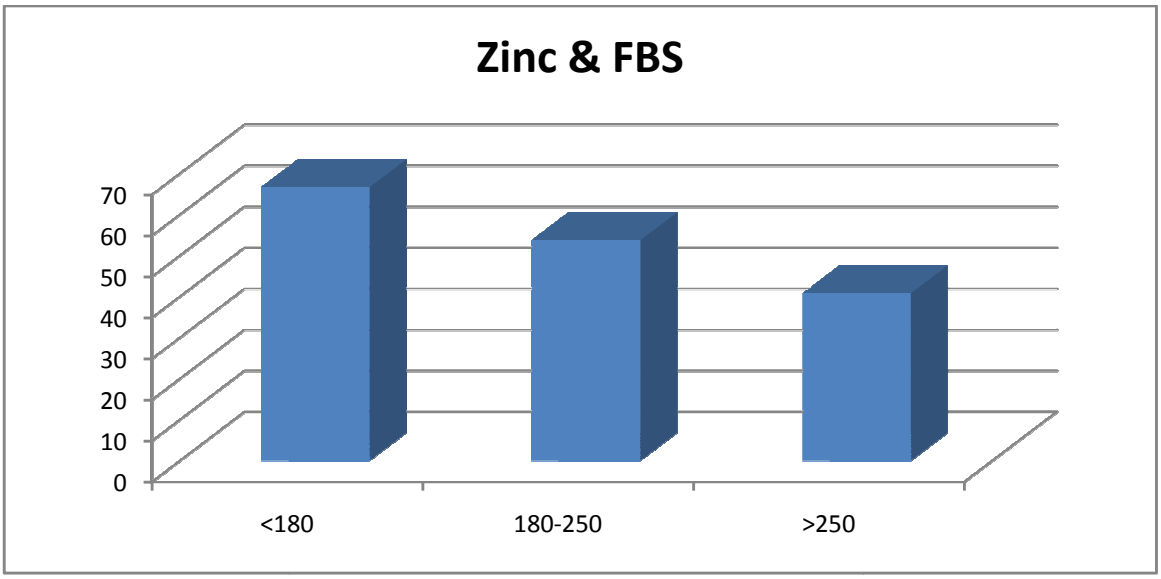


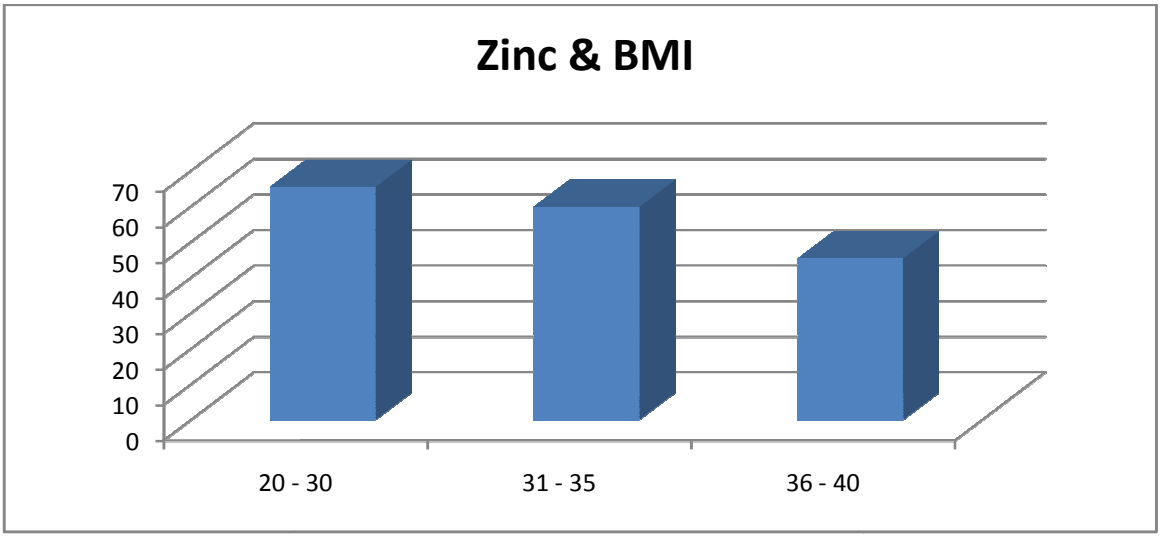
Figure 27 – FBS and Zinc correlation

Correlation of Zinc with BMI in diabetes

Table 21 - Zinc and BMI correlation

BMI	No of diabetes	Mean Zinc value
20 – 30	15	65.48
30 – 35	24	59.9
35 – 40	11	45.33

In our study diabetes is divided in to three group based on BMI . Mean zinc value decreases with increase in BMI and statistically significant (p value <0.001).Pearson correlation coefficient for zinc and BMI in diabetes and control are -0.492 and -0.161 respectively and correlation is higher for diabetes than control.



Figue 28 – BMI and Zinc correlation

Correlation of Zinc and Triglyceride in diabetes

Table 22 – Zinc and Triglyceride correlation

Triglyceride	No of diabetes	Mean Zinc value
≤150	13	68.07
151– 250	28	58.38
>250	9	42.48

Mean zinc value decreases with increase in triglyceride value in diabetes and it is statistically significant (p value 0.001).Pearson correlation coefficient for zinc and triglyceride in diabetes and control are -0.451 and -0.045 respectively and correlation is higher for diabetes than control

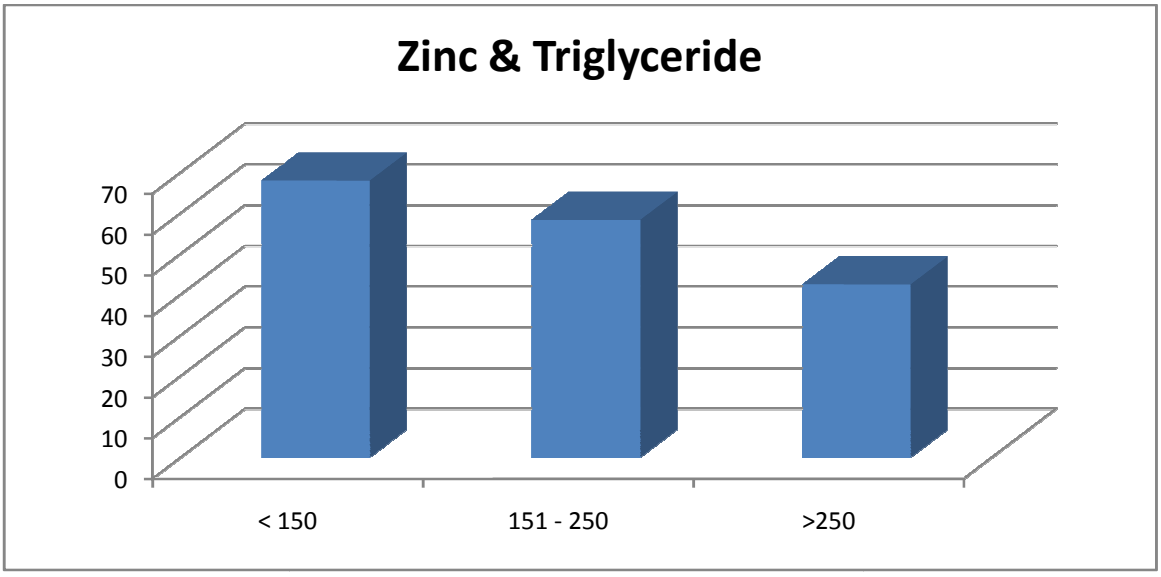


Figure 29 – Zinc and Triglyceride correlation

Correlation of Zinc and cholesterol in diabetes

Table 23 – Zinc and Cholesterol correlation

Cholesterol	No of diabetes	Mean Zinc value
≤ 200	18	64.75
201 – 250	14	63.77
>250	18	45

In our study mean zinc value decreases with increase in cholesterol in diabetes and it is statistically significant.Pearson correlation coefficient for zinc and cholesterol in diabetes and control are -0.422 and -0.046 respectively and correlation is higher for diabetes than control.

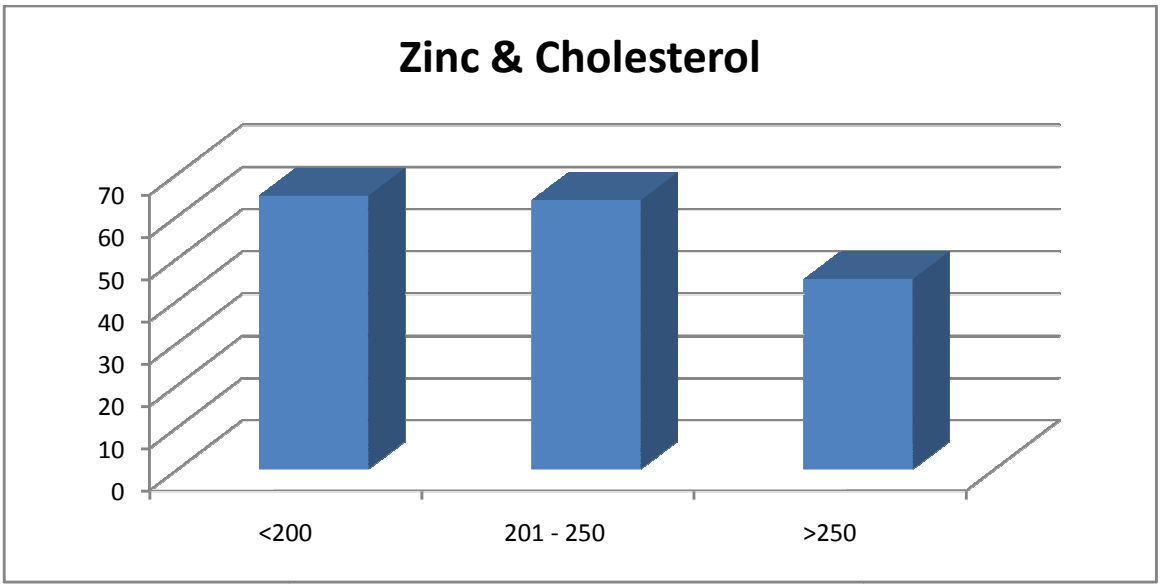


Figure 30 – zinc and cholesterol correlation

Correlation of Zinc and Blood Pressure in diabetes

Table 24 – Zinc and SBP correlation

Systolic blood pressure	No of diabetes	Mean Zinc value
≤ 120	8	69.12
121 – 140	31	58.29
>140	11	51.8

Table 25 – Zinc and DBP correlation

Diastolic blood pressure	No of diabetes	Mean Zinc value
≤ 80	24	64.5
80 – 90	19	53.2
>90	7	50.7

In our study mean zinc value decreases with increase in blood pressure in diabetes. Pearson correlation coefficient for zinc and systolic blood pressure in diabetes and control are -0.351 and -0.103 respectively and correlation is higher for diabetes than control.Pearson correlation coefficient for zinc and diastolic blood pressure in diabetes and control are -0.422 and -0.146 respectively and correlation is higher for diabetes than control

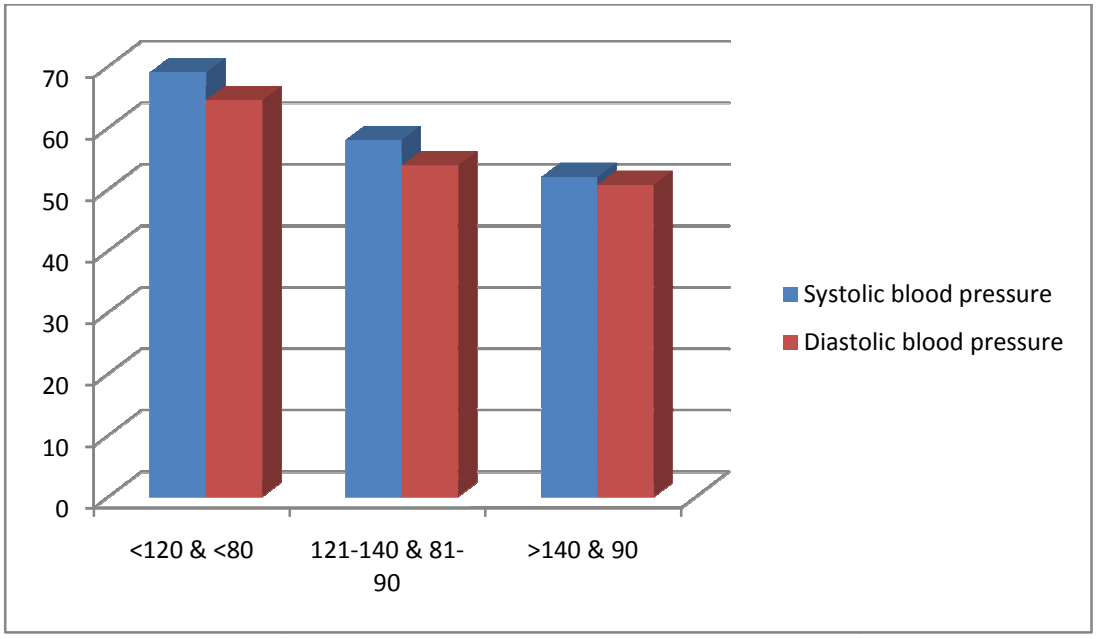


Figure 31 – Correlation of Zinc with SBP / DBP

DISCUSSION

Discussion

In our study 100 patients (50 diabetic and 50 control) were subjected to history, examination and investigations after getting their consent.only newly diagnosed type 2 DM without complications attending medicine department were included as cases in the study.

It wasobserved mean HbA1c, fasting blood sugar, hypertension, body mass index, triglyceride, cholesterol, systolic blood pressurein diabetes were found to be significantly higher than control. Urea, creatinine and diastolic blood pressure were not statistically significant. This showed diabetes have increased association with dyslipidemia , hypertension and obesity than control. Insulin resistance and other unknown mechanism was involved in pathogenesis of this association.

Zinc and HbA1c

Mean zinc value of diabetes was 58.31 $\pm$17.23 significantly lower than control (75.65 $\pm$ 18.05) and it was statistically significant (p value <0.001). This correlated with study conducted by McNair et al., in his study serum zinc was inversely related to glycemic status of diabetes. Garg et al ., also reported similar findings in diabetes. Williams et al., observed 17% decrease in Zinc concentration in diabetes while comparing with controls.[21]

In our study pearson correlation coefficient of Zinc and HbA1c in diabeteswas -0.543 which established strong negative correlation and statistically significant (p value < 0.001) whereas correlation coefficient of control for these two parameters was -0.120 and not significant (p value 0.408).

Tripathy et al., in his study showed negative correlation between Zinc and HbA1c with 'r' value of -0.408.[22]

Zinc & Fasting blood glucose

In our study mean fasting blood sugar was significantly higher in diabetic than control and pearson correlation coefficient of zinc and FBS showed significant negative correlation in diabetes (- 0.553)compared to control (- 0.084). our study showed serum zinc deficiency occur with increase in glycemic status..

Zinc and Obesity

In our study mean BMI was significantly higher in diabetes than control. our study showed obesity was associated with type 2 DM. Association between diabetes and obesity was shown by many studies . Mokdad et al., in his study showed strong association between DM and BMI using data from Behavioral Risk Factor Surviellance System.[23].

Our study also showed negative correlation between BMI and zinc in diabetes .

Zinc and dyslipidemia

Triglyceride and cholesterol were significantly higher in diabetes than control in our study which shows association between dyslipidemia and type 2 DM. Insulin resistance in DM was well known reason for dyslipidemia. Zinc had negative correlation with triglyceride and cholesterol in diabetes in our study .There was only limited study about zinc and dylipidemia and more studies were needed to confirm this relationship.

Zinc and hypertension

In our study systolic blood pressure was significantly higher in diabetes than control whereas diastolic blood pressure was not statistically significant. Negative correlation was seen between zinc and systolic /diastolic blood pressure in diabetes.

Our study showed zinc deficiency occur with increased glycemic status. There was also association between zinc and obesity/dyslipidemia/ hypertension in diabetes .Large scale studies were needed to prove correlation between zinc and obesity/dyslipidemia/hypertension.

Studies had shown zinc deficiency in diabetes increase and fasten both micro and macrovascular complications. So detecting zinc deficiency in diabetes earlier help in preventing complications and also controlling glycemic status.

In 2006 Al-Maroof et al., study showed zinc supplementation had beneficial effects in improving glycemic control in diabetes. His study included 133 diabetic cases and they were given zinc supplementation for 3 months which showed significant decrease in HbA1c[24]

In 2007 Beletate et al., study showed no evidence of zinc supplementation in preventing type 2 DM from insulin resistance.[25]. This study included 128 insulin resistance cases and they were given zinc supplementation for 3 months.

Large scale studies are needed to support zinc supplementation in type 2 DM to control blood glucose.

CONCLUSIONS

Conclusion

1. Zinc deficiency is significantly higher in diabetes than control.
2. Zinc has strong negative correlation with HbA1c. zinc level decreases with increase in HbA1c.
3. Zinc has strong negative correlation with FBS. zinc level decreases with increase in FBS.
4. Obesity, Systolic hypertension and dyslipidemiaare more frequent in diabetes than control.
5. Zinc also has negative correlation with obesity/ hypertension / dyslipidemia in diabetes in our study.

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BIBLIOGRAPHY

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.Ganesh V
Postgraduate M.D.(General Medicine)
Madras Medical College
Chennai 600 003

Dear Dr.Ganesh V,

The Institutional Ethics Committee has considered your request and approved your study titled **"Study of serum zinc status and glycated haemoglobin in Type 2 Diabetes Mellitus" No.25042015.**

The following members of Ethics Committee were present in the meeting held on 07.04.2015 conducted at Madras Medical College, Chennai-3.

1. Prof.C.Rajendran, M.D.,	: Chairperson
2. Prof.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4. Prof.B.Vasanthi, M.D., Prof. of Pharmacology, MMC	: Member
5. Prof.P.Ragumani, M.S., Professor of Surgery, MMC	: Member
6. Prof.S.Baby Vasumathi, Director, Inst. Of O&G, MMC	: Member
7. Prof.K.Ramadevi, Director, Inst.of Biochemistry, MMC	: Member
8. Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3	: Member
9. Prof.K.Srinivasagalu, M.D.,Director, I.I.M. MMC, Ch-3	: Member
10.Thiru S.Rameshkumar, B.Com., MBA	: Lay Person
11.Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
12.Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

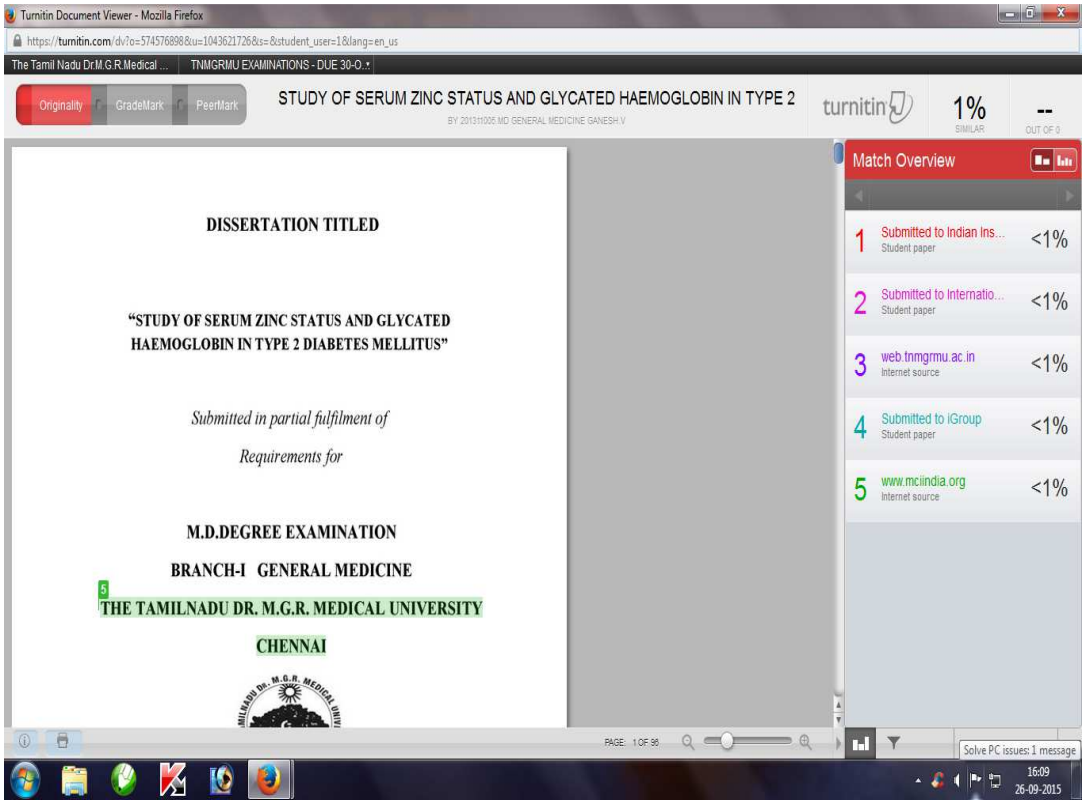
We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

8/4/15

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003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Submitted in partial fulfilment of
Requirements for
M.D.DEGREE EXAMINATION
BRANCH-I GENERAL MEDICINE
THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
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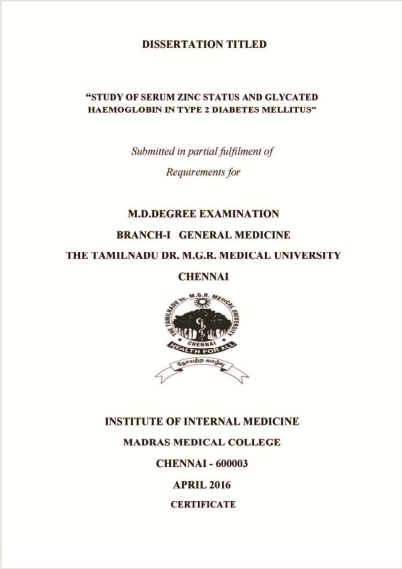

DISSERTATION TITLED

"STUDY OF SERUM ZINC STATUS AND GLYCATED HAEMOGLOBIN IN TYPE 2 DIABETES MELLITUS"

Submitted in partial fulfilment of
Requirements for

M.D.DEGREE EXAMINATION
BRANCH-I GENERAL MEDICINE
THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI

INSTITUTE OF INTERNAL MEDICINE
MADRAS MEDICAL COLLEGE
CHENNAI - 600003
APRIL 2016
CERTIFICATE

ANNEXURES

"Study of Serum Zinc status and Glycated Hemoglobin in Type 2 Diabetes Mellitus":

PROFORMA

Name: Age/Sex:
Address: Occupation:

SYMPTOMS:

PAST HISTORY:

PERSONAL HISTORY:
SMOKING
ALCOHOL

FAMILY HISTORY:

TREATMENT HISTORY:

GENERAL EXAMINATION:

GCS	

VITAL SIGNS:

PR-
BP-
RR-

HEIGHT -
WEIGHT-
BMI-

SYSTEMIC EXAMINATION:

CVS:

RS:

ABDOMEN:

CNS:

EYE:

INVESTIGATIONS:

SERUM ZINC :

HbA1c :

FASTING BLOOD GLUCOSE :

SERUM UREA :

SERUM CREATININE :

SERUM TRIGLYCERIDE:

SERUM CHOLESTEROL:

ELECTROCARDIOGRAM:

INFORMATION SHEET

We are conducting a study on **"Study of Serum Zinc status and Glycated Hemoglobin in Type 2 Diabetes Mellitus"** among patients attending medicine outpatient department in Rajiv Gandhi Government General Hospital, Chennai and for that your specimen may be valuable to us.

The purpose of this study is to assess serum Zinc level and to compare with glycated hemoglobin in Type 2 Diabetes mellitus and healthy sujects .

We are selecting patients based on criteria and if you are found eligible, we may be using your blood samples to do tests which includes serum Zinc, HbA1c, fasting blood glucose,triglyceride,cholesterol, serum urea and creatinine which in any way do not affect your management.

Thorough history and clinical examination will be done on patients who are selected and above mentioned tests will be done on day 1 and one fasting blood sample will be taken .

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator | Signature of Participant

Date :
Place :

ஆராய்ச்சி தகவல் தாள்

சென்னை இராஜிவ் காந்தி அரசு பொது மருத்துவமனையில் பற்றிய ஒரு ஆராய்ச்சி நடைபெற்று வருகிறது.

டைப் 2 நீரிழிவு நோயாளிகளின் இரத்தத்தில் ஜிங்க் மற்றும் எச்பிஏ1சி அளவு பார்ப்பதே இந்த ஆராய்ச்சியின் நோக்கமாகும்.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். முடிவுகளை அல்லது கருத்துக்களை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருத்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவில் தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி:

PATIENT CONSENT FORM

Study Detail	:	"Study of Serum Zinc status and Glycated Hemoglobin in Type 2 Diabetes Mellitus"
Study Centre	:	Rajiv Gandhi Government General Hospital, Chennai.
Patient's Name	:	
Patient's Age	:	
Identification Number	:	

Patient may check (√) these boxes

a) I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ❑

b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ❑

c) I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ❑

d) I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ❑

e) I hereby consent to participate in this study. ❑

f) I hereby give permission to undergo detailed clinical examination and blood investigations as required. ❑

Signature/thumb impression	Signature of Investigator
Patient's Name and Address:	Study Investigator's Name: **Dr. V.Ganesh**

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு:

டைப் 2 நீரிழிவு நோயாளிகளின் இரத்தத்தில் ஜிங்க் மற்றும் எச்பிஏ1சி அளவு பார்ப்பதே இந்த ஆராய்ச்சியின் நோக்கமாகும்.

பெயர்: தேதி:

வயது: உள்நோயாளி எண்:

பால்: ஆராய்ச்சி சேர்க்கை எண்:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது. எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்து கொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

டைப் 2 நீரிழிவு நோயாளிகளின் இரத்தத்தில் ஜிங்க் அளவு குறைவாக உள்ளது பற்றியும் அதனைக் கண்டறிய மேற்கொள்ளப்படும் பரிசோதனைகளைப் பற்றியும் ஆராய்ச்சியாளர் கூற முழுவதும் விளங்கப்பெற்றேன்

மேற்கொண்ட பரிசோதனையின் போது ஏற்படக்கூடிய பின்விளைவுகளையும் முழுவதும் உணர்ந்து இந்த பரிசோதனைக்கு மனமார சம்மதிக்கிறேன்.

கையொப்பம்

MASTER CHART

MASTER CHART FOR DIABETES

S.NO	AGE	SEX	HBA1C	FBS	UREA	Creatinine	BMI	Triglyceride	Cholesterol	BP	Zinc
1	40	F	14.8	326	36	1.1	34.3	230	310	130/80	43.9
2	41	M	10.2	240	26	0.4	33.6	160	174	126/82	42.6
3	41	M	9.9	223	27	0.8	28.1	145	255	120/80	37.8
4	58	M	7.3	160	18	0.9	32.4	180	188	136/84	42.4
5	45	F	11.1	155	30	0.5	36.5	245	284	150/96	32.4
6	60	F	7.5	170	33	0.9	27	120	210	126/74	77.8
7	60	F	7.9	120	48	1.2	33.4	186	164	130/80	75.2
8	45	F	6.7	111	34	0.8	34.2	173	192	142/90	66.5
9	50	M	10	196	50	1.1	29.8	210	156	128/72	77.8
10	46	M	9.6	210	42	0.8	33.1	330	246	140/90	50.1
11	44	F	8.2	136	44	0.5	27.6	126	156	118/70	70
12	55	F	7.4	140	34	0.9	28.4	137	178	120/80	93.6
13	42	M	8.6	156	36	0.6	35.3	238	210	150/96	68.1
14	41	M	10.8	230	38	0.8	32.9	294	255	134/82	43.9
15	55	M	11.6	290	46	1	36.4	248	226	140/90	36.3
16	60	M	7	116	14	1.3	29.2	110	184	126/78	82.1

17	47	F	6.8	124	24	0.9	30.3	148	198	134/80	64.7
18	56	M	7.3	139	28	0.7	33.1	142	226	144/82	72.5
19	58	F	8.8	178	36	0.9	33.8	166	245	134/70	92.4
20	44	F	8.1	167	27	0.9	37.5	258	288	154/98	30.6
21	55	M	7.9	157	35	0.9	32.4	248	178	126/78	47.8
22	47	F	7.8	180	36	0.6	32.1	184	253	130/80	55.9
23	41	F	8.9	199	42	0.7	38	278	326	156/90	33
24	44	M	8.6	186	44	1.1	30.6	142	237	126/88	47.6
25	48	M	7.1	166	36	0.8	29.7	112	178	138/82	72.8
26	43	F	6.9	123	24	0.9	30.4	178	212	126/78	86.7
27	40	F	10	303	36	1	35.4	164	273	140/90	40.2
28	40	M	9.3	220	28	0.5	32.7	189	214	118/70	66.7
29	54	F	8.2	210	30	0.7	27.4	135	124	110/70	64.9
30	56	M	11.3	320	30	0.9	36.4	178	346	124/86	36.9
31	60	F	8.4	193	34	1.2	33.5	220	223	128/78	74.5
32	59	F	7.6	148	36	0.9	29.3	246	176	112/74	76.9
33	42	M	8.6	164	37	0.6	27.1	214	192	114/68	45.8
34	45	F	8.8	178	41	0.6	35.3	256	269	136/78	39.5

35	47	M	9	207	20	0.9	34.8	186	314	134/76	42.3
36	42	M	6.8	130	40	0.5	36.2	234	295	146/94	85.2
37	50	M	7.2	156	42	0.8	28.4	128	198	110/72	55.9
38	52	F	7.7	163	33	1.1	33.2	258	255	126/78	57.3
39	46	F	7.9	175	31	0.9	31.7	196	214	136/84	64.5
40	48	M	8.1	168	28	0.7	31.2	188	229	134/86	67.2
41	44	M	8.8	194	32	0.7	37.9	194	294	152/94	35.9
42	56	M	8	190	27	0.9	34.2	228	263	140/90	54.2
43	42	M	7.9	202	34	1.1	27.6	204	146	128/78	49.8
44	47	F	9.9	267	36	0.9	38.2	312	278	154/94	41.6
45	43	F	8.7	254	36	0.6	34.5	231	244	140/90	45.9
46	40	M	8.3	241	40	0.5	39.1	246	285	156/94	51.4
47	51	M	7.9	220	22	0.7	33.2	173	176	134/86	63.9
48	53	F	7.4	182	20	0.9	28.9	178	153	132/86	65.4
49	44	F	7.5	177	18	1	26.3	137	189	118/78	79.2
50	47	F	8.4	210	26	0.7	31.7	146	209	124/82	66.1

MASTER CHART FOR CONTROL

1	47	F	5.4	104	38	0.5	24.7	110	144	104/68	62.9
2	49	M	5.2	93	38	0.6	25.6	136	176	110/72	88.4
3	55	F	4.9	100	37	0.9	27	128	188	114/70	52.4
4	42	M	5.7	70	28	0.8	27.3	194	214	124/76	80.2
5	52	F	5.9	93	20	0.8	25.2	220	146	120/80	76.4
6	49	M	5.5	84	30	0.7	24.8	178	199	120/80	45.2
7	48	F	5.5	80	24	1	33.1	184	234	132/82	68.4
8	44	F	5.6	110	44	0.9	33.8	247	267	140/90	93.9
9	57	F	5.4	111	21	1.1	29.4	124	174	126/82	84.8
10	54	F	5.2	86	42	1.2	22.6	118	114	118/70	78.5
11	43	M	5.1	89	26	0.7	28.4	104	163	122/80	74.2
12	46	F	5.3	74	26	0.7	29.4	206	210	124/84	37.8
13	45	M	5.3	99	34	0.5	31.1	213	232	138/88	80.2
14	56	M	4.5	73	30	0.6	30.6	147	192	126/78	76.3
15	59	F	5.4	81	14	0.9	34.7	188	279	130/80	56.7
16	42	F	5.5	84	18	1.1	31.8	218	310	136/88	77.9
17	47	F	5.8	107	29	0.9	27.4	130	175	116/72	112.4
18	48	F	5.4	96	34	0.6	30.6	136	213	128/72	85.2
19	51	M	5.4	85	35	0.7	21.4	88	176	100/66	90.2
20	54	M	5.7	95	39	0.8	30.3	126	145	128/84	47.6

21	54	F	5.8	94	36	1.1	33.4	164	260	130/80	49.2
22	48	F	5.5	117	29	0.6	26.3	139	194	120/80	70.1
23	42	M	5.5	76	40	0.5	25.3	150	166	118/74	120.6
24	41	F	6.1	119	44	0.5	28.4	155	124	118/76	54.9
25	54	M	4.8	82	42	0.6	29.7	163	204	126/80	78.3
26	57	M	5.2	76	34	1.1	30.8	200	194	130/84	85.6
27	40	M	5.5	81	31	0.9	33.1	224	259	136/86	94.3
28	52	M	5.1	84	20	0.8	36.2	294	231	150/96	66.2
29	48	F	6.1	108	26	0.8	26.5	168	193	120/80	114.5
30	45	F	5.5	96	28	0.6	27.8	163	178	118/76	82.3
31	44	M	5.8	110	43	0.6	28	157	257	132/78	63.9
32	49	M	5.5	84	28	0.7	29.3	268	304	120/80	73.8
33	51	F	4.8	88	31	1.2	30.4	273	326	136/78	82.6
34	60	F	5.3	88	28	0.9	31.2	203	182	146/92	90.5
35	44	F	5.7	94	29	0.5	31.8	194	234	120/80	84.5
36	50	M	5.5	78	30	0.4	28.8	169	134	108/70	77.1
37	59	F	5.8	99	31	1.2	29.7	184	166	126/74	57.8
38	40	M	6.3	116	33	0.6	30.2	158	146	128/80	49.8
39	45	F	5.2	92	40	0.8	37.6	194	267	142/90	66.4
40	46	M	5.4	83	41	1	32.8	234	198	146/82	72.1
41	53	F	4.6	96	32	0.7	32.4	312	288	124/78	94.8
42	57	M	5.5	104	24	0.9	27.6	124	210	124/78	65.3

43	41	F	4.9	76	25	0.5	27.1	117	180	118/72	116.4
44	45	M	5.4	108	28	0.9	30.5	168	248	136/90	74.9
45	55	F	5.1	94	26	0.6	24.3	111	158	100/74	83.1
46	58	F	5.2	88	16	0.8	27.5	108	166	120/80	62.9
47	40	M	5.3	81	28	0.9	28.4	94	154	124/84	62.4
48	42	M	5	96	20	0.8	29.2	145	164	132/86	70.4
49	54	M	5.1	78	14	0.9	30.2	186	188	126/80	72.9
50	60	F	6.3	102	40	0.9	34.2	238	224	154/94	75.6

FBS fasting blood sugar 70 - 125mg/dl

BP blood pressure <140/90

HBA1C <6.5

Zinc 70 -150 microgram/dl

Triglyceride <150mg/dl

Cholesterol<200mg/dl

BMI body mass index <23